THE American JOURNAL OF Surgery

JULY 1955

THURSTON SCOTT WELTON, M.D., EDITOR

Resection of the Colon

Bronchopulmonary Diseases

Intravenous Cholangiography

SIXTY-FOURTH YEAR OF PUBLICATION

JULY 1955

THE American JOURNAL OF Surgery

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The American Journal of Surgery

CONTENTS–July 1955

VOLUME NINETY NUMBER ONE

EDITORIAL

Motorist Injuries 1

JACOB KULOWSKI

SCIENTIFIC PAPERS

Intravenous Cholangiography 4

GONZALO ESGUERRA-GÓMEZ AND ALFONSO CASTRO-RIAÑO

Since cholecystography and oral cholangiography do not permit visualization of the biliary ducts when the gallbladder fails to visualize or when the patient has been cholecystectomized, the authors recommend that cholografin be employed routinely in intravenous cholangiography. This method is recommended in these cases; otherwise the oral procedure gives as good results. Toleration and results obtained are given.

Complications from Resection of the Colon. An Evaluation of Complementary Cecostomy . . . 12

J. MALCOLM EDMISTON AND W. BIRNBAUM

The authors review the complications arising from 226 cases of resection of the colon for various types of lesions. Only nonobstructive cases of primary anastomosis distal to the ascending colon are considered. The authors conclude that complementary cecostomy is still a useful procedure and should be considered when ideal conditions for bowel anastomosis are not present.

Contents Continued on Page 5

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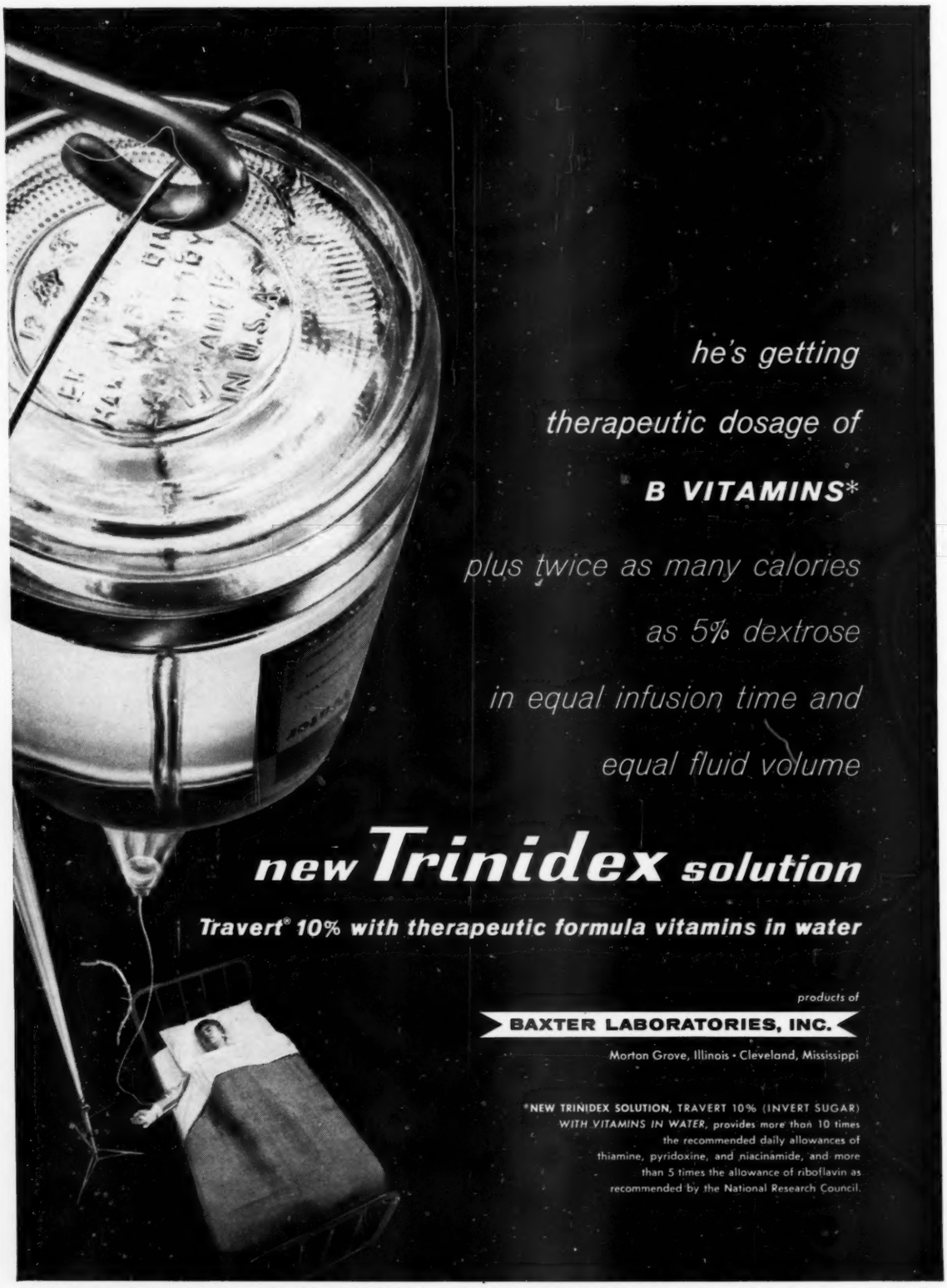
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CONTENTS continued–July 1955

VOLUME NINETY NUMBER ONE

Congenital Aganglionic Megacolon 18

HAROLD AXELROD

The author discusses the history, pathologic physiology, clinical course, diagnosis and technic of operation for the cure of congenital aganglionic megacolon. Two illustrative case reports are included.

Gastrointestinal Adenosis Associated with Melanin Spots on Lips, Buccal Mucosa and Digits . . . 26

JOSEPH P. O'BRIEN

A case of hereditary adenosis of the gastrointestinal tract associated with distinctive melanin spots on the lip, buccal mucosa and digits has been added to the number already reported.

Segmental Resection for Tuberculosis. Analysis of Fifty Consecutive Cases 32

ALBERT H. ST. RAYMOND, JR. AND FRANCIS H. COLE

Fifty consecutive cases of segmental resection for pulmonary tuberculosis have been reviewed and analyzed. There were no deaths. Necessary preoperative studies, operative technic and postoperative care are discussed. The conclusion drawn is that segmental resection is a valuable procedure in selected cases.

Cancer of the Breast 37

RICHARD A. LEONARDO

The author gives his reasons for use of certain surgical treatments and x-ray therapy, with end results, in various stages of malignancy of the breast.

The Use of Clorpactin WCS 90 As an Antiseptic in Surgery 44

WILSON A. SWANKER

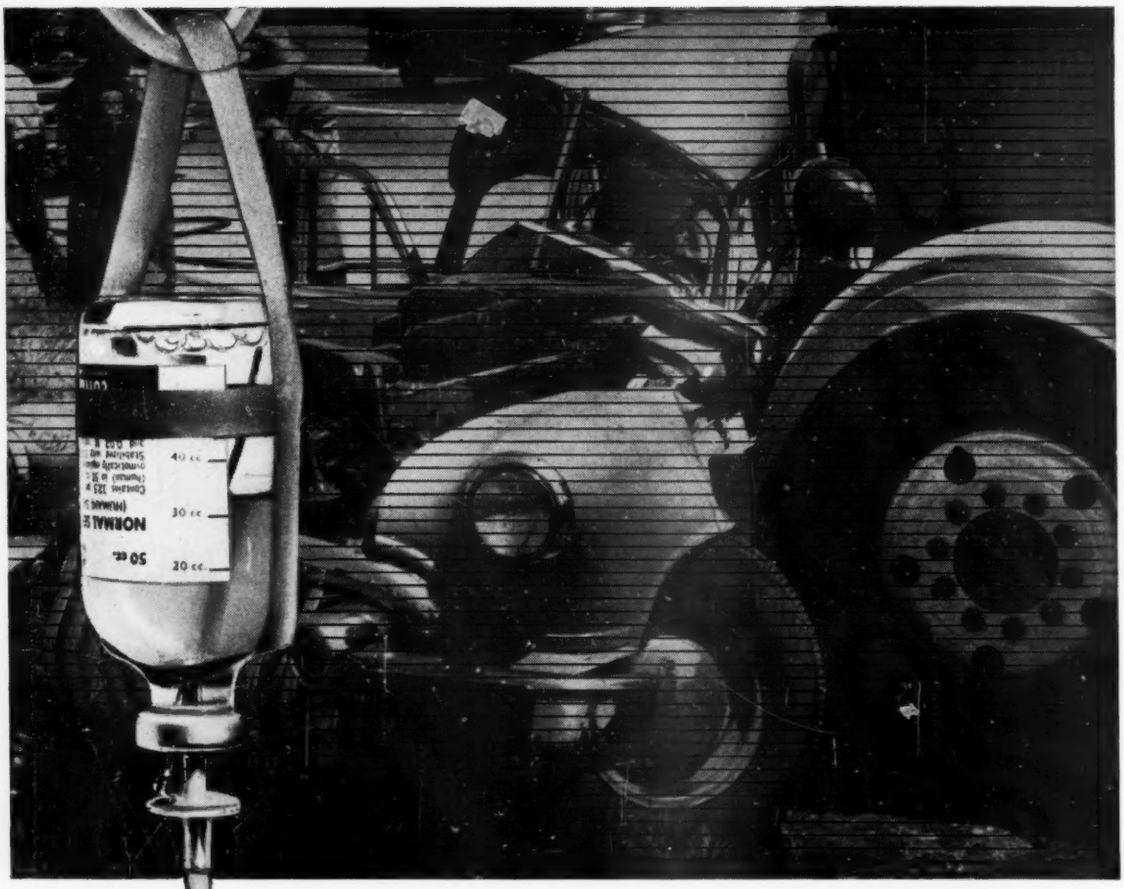
A breakdown of the results in a series of 164 surgical procedures performed using 0.25 per cent aqueous solution of clorpactin WCS 90 for pre- and postoperative antisepsis.

Control of Postpartum Lochia with Kutapressin . 47

WALLACE MARSHALL, A. WM. KOZELKA AND DOMINIC A. KULJIS

A new non-toxic selective vasoconstrictor, according to the authors, was used successfully in sixty-eight consecutive postpartum cases to suppress and shorten the time of lochial discharges.

Contents Continued on Page 7



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CONTENTS continued–July 1955

VOLUME NINETY NUMBER ONE

BRONCHOPULMONARY DISEASES—SYSTEMIC DISEASES, FUNGOUS INFECTIONS, PNEUMOCONIOSES

Pulmonary Manifestations of Systemic Diseases . 50
ELI H. RUBIN

Pulmonary Roentgenologic Changes in the Collagen Diseases 63
L. H. GARLAND AND M. A. SISSON

The Mycotic Infections of the Bronchial-Pulmonary Tract 77
ARTHUR Q. PENTA

Pulmonary Histoplasmosis 92
LT. COL. THOMAS F. PUCKETT

Surgical Considerations in Pulmonary Coccidioidomycosis. Report of 100 Cases 101
BERT H. COTTON, GEORGE A. PAULSEN AND J. W. BIRSNER

The Pathogenesis and Management of Pneumoconiosis 107
ARTHUR J. VORWALD

Silicosis and Asbestosis. Diagnosis, Prevention and Treatment 115
O. A. SANDER

Beryllium Poisoning (Beryllosis). X-ray Manifestations and Advances in Treatment 120
H. E. TEBROCK

These articles are a continuation of the Symposium featured in the January and February issues. The articles in this issue cover the subjects of systemic diseases, fungous infections and pneumoconioses.

PRACTICAL SURGICAL SUGGESTIONS

Transvaginal Pelvioscopy (Peritoneoscopy). A Simplified and Safe Technic As an Office Procedure. . 122
A. R. ABARBANEL

Contents Continued on Page 9

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CONTENTS continued–July 1955

VOLUME NINETY NUMBER ONE

Simple Coupling Methods for Polyethylene Tubing . 129
SIDNEY HIRSCH

Shoulder Pendulum Exerciser 130
LASZLO ORMANDY

An Important Diagnostic Aid in Rectal Examination. The Value of Straining in the Squatting Position 132
DANIEL J. ABRAMSON

CASE REPORTS

Surgical Management of Unusual Anorectal Lesions 134
JOHN R. STEEPER AND GEORGE H. EWELL

Four unusual anorectal lesions are presented and discussed. Each was a special problem in treatment, and the surgical management illustrates some of the less commonly used methods of resection of the rectum.

Neurilemmoma of the Sigmoid Colon, Associated with Diverticulitis As a Cause of Obstruction . . 139
MELFORD B. JORGENSEN

The author reports a most unusual condition, a case of neurilemmoma of the sigmoid colon associated with diverticulitis causing obstruction.

Intraperitoneal Perforation of Infected Urachal Cyst 143
LT. COL. RALPH P. CAMPANALE
AND CAPT. RONALD W. KRUMBACH

A case is reported of an acute abdominal syndrome caused by the intraperitoneal perforation of an infected urachal cyst (rare in adults).

Buschke-Loewenstein Tumors (Giant Condylomata Acuminata) 146
WILLIAM DREYFUSS AND WILLIAM E. NEVILLE

A case is presented of giant condylomata acuminata with extensive destruction of penile skin and expansion into one corpus cavernosum. Technic of operation is given and the pathology, nomenclature and treatment are discussed.

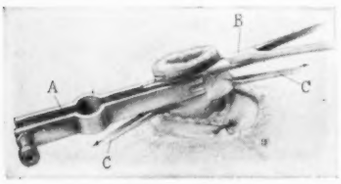
An Unusual Urethral Fistula Site 151
A. ESTIN COMARR AND ERNEST BORS

Two cases of unusual urethral fistula have been presented which were complications of bilateral removal of the ischium.

Contents Continued on Page 11

The Daniel Colostomy Clamp

This versatile clamp has proved itself of value in single, double-barreled, Mikulicz and Devine colostomies, as well as in cecostomy and ileotomy. It is a distinct aid in early decompression of an obstructed bowel, minimizing or eliminating bowel distention, nausea, vomiting or ileus. Its use permits early ingestion of foods and fluid, as well as allows the patient freedom of movement with comfort and safety. The technic also prevents danger of bowel perforation, soiling of the wound by bowel contents, tearing of the bowel by accidental traction, and retraction of a short colostomy before firm adherence to the abdominal wall.



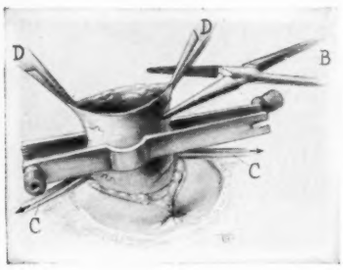


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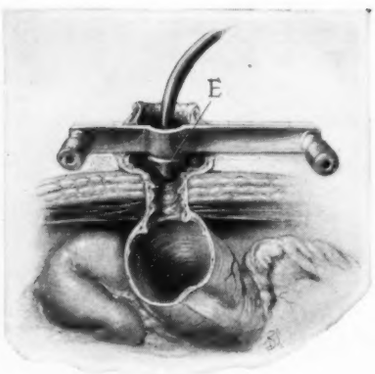
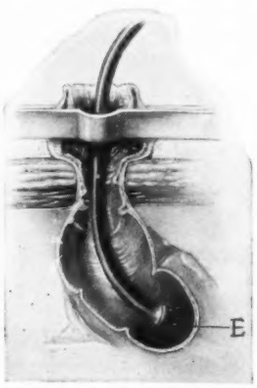
Fig. 1—Wound closed and dressed around terminal bowel, forming colostomy. Daniel clamp (A) placed between large clamp (B) and two Allis clamps (C). *Fig. 2*—Daniel clamp (A) in place; bowel edges separated, held by Kelly forceps (D); original clamp (B) removed. *Fig. 3*—Size 28 or 30 soft-nose mushroom catheter (E) being inserted into bowel lumen. *Fig. 4*—Head of catheter is just below locked clamp. *Fig. 5*—Mushroom catheter advanced into abdominal portion of bowel under pressure of enema water.





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CONTENTS continued–July 1955

VOLUME NINETY NUMBER ONE

Incomplete Cholecystogastric Fistula 153

BRUCE E. CHAMBERLAIN

A unique case report of incomplete cholecystogastric fistula. This case has been shown to be a problem of diagnosis in respect to gastrointestinal hemorrhage and gastric neoplasm.

Stability Following Hip Resection for Infection . . 155

PETER L. CARNESALE, OWEN E. MILLER AND EDWARD K. RATH

Two cases of resection of the hip are described which resulted in strong and stable joints without further surgical intervention. The postoperative infection was the common factor in this result.

BOOK REVIEWS. 159

NOTES AND QUOTES (Advertising Section) . . 40

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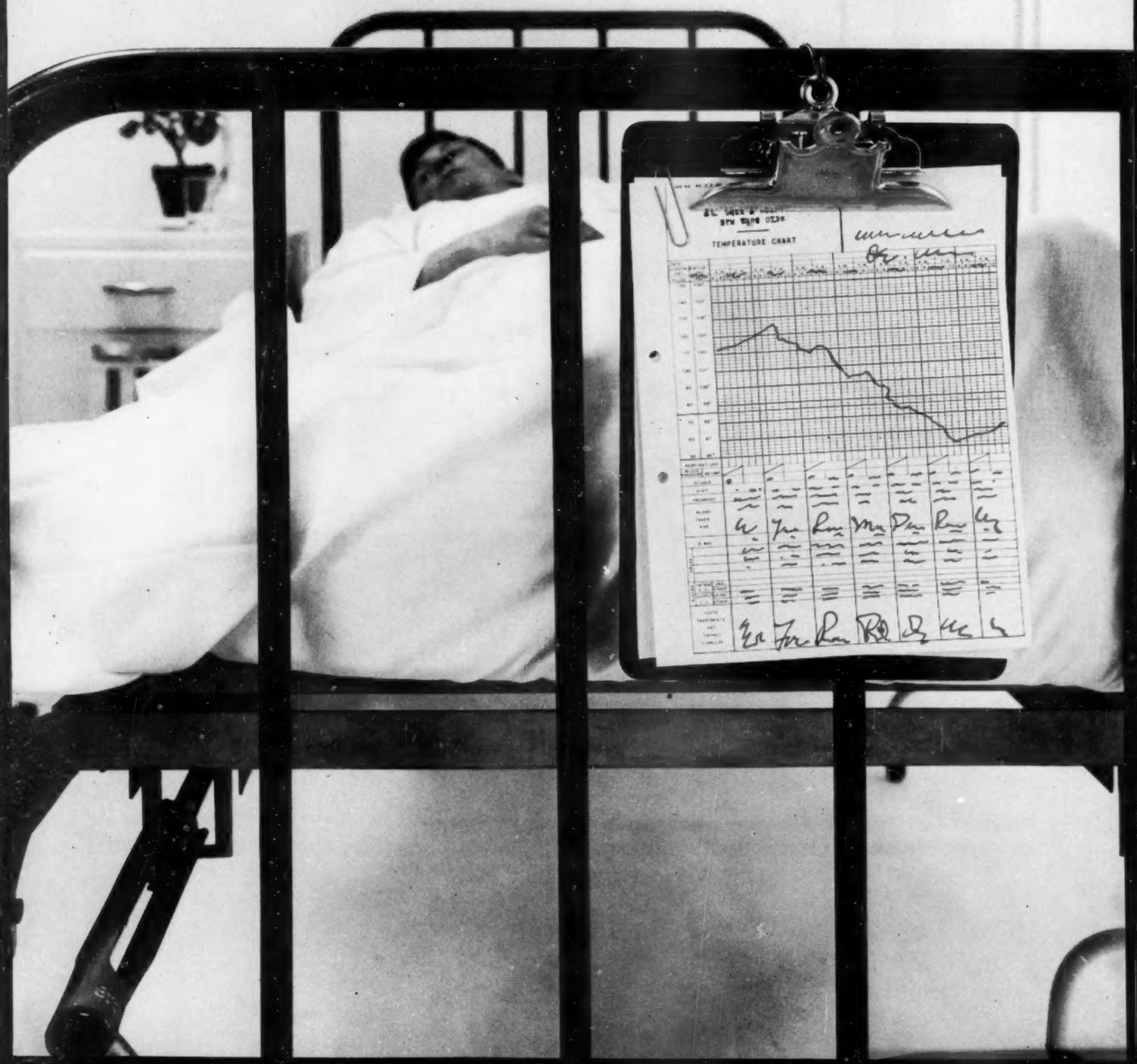

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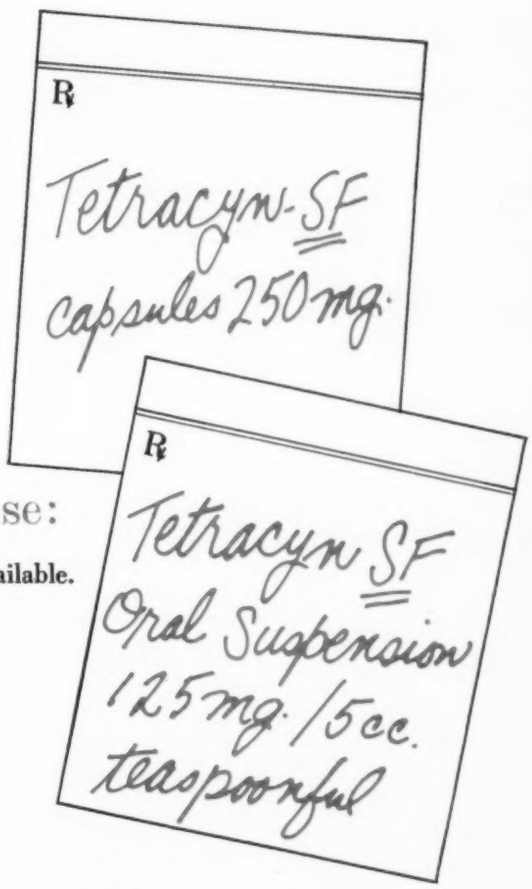

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1. Pollack, H., and Halpern, S. L.: Therapeutic Nutrition, Prepared in Collaboration with the Committee on Therapeutic Nutrition, Food and Nutrition Board, National Research Council, Washington, D. C., 1952.
2. Martí-Ibáñez, F: Antibiotic Med. *1*:247 (May) 1955.
3. Dumas, K. J.; Carlozzi, M., and Wright, W. A.: Antibiotic Med. *1*:296 (May) 1955.

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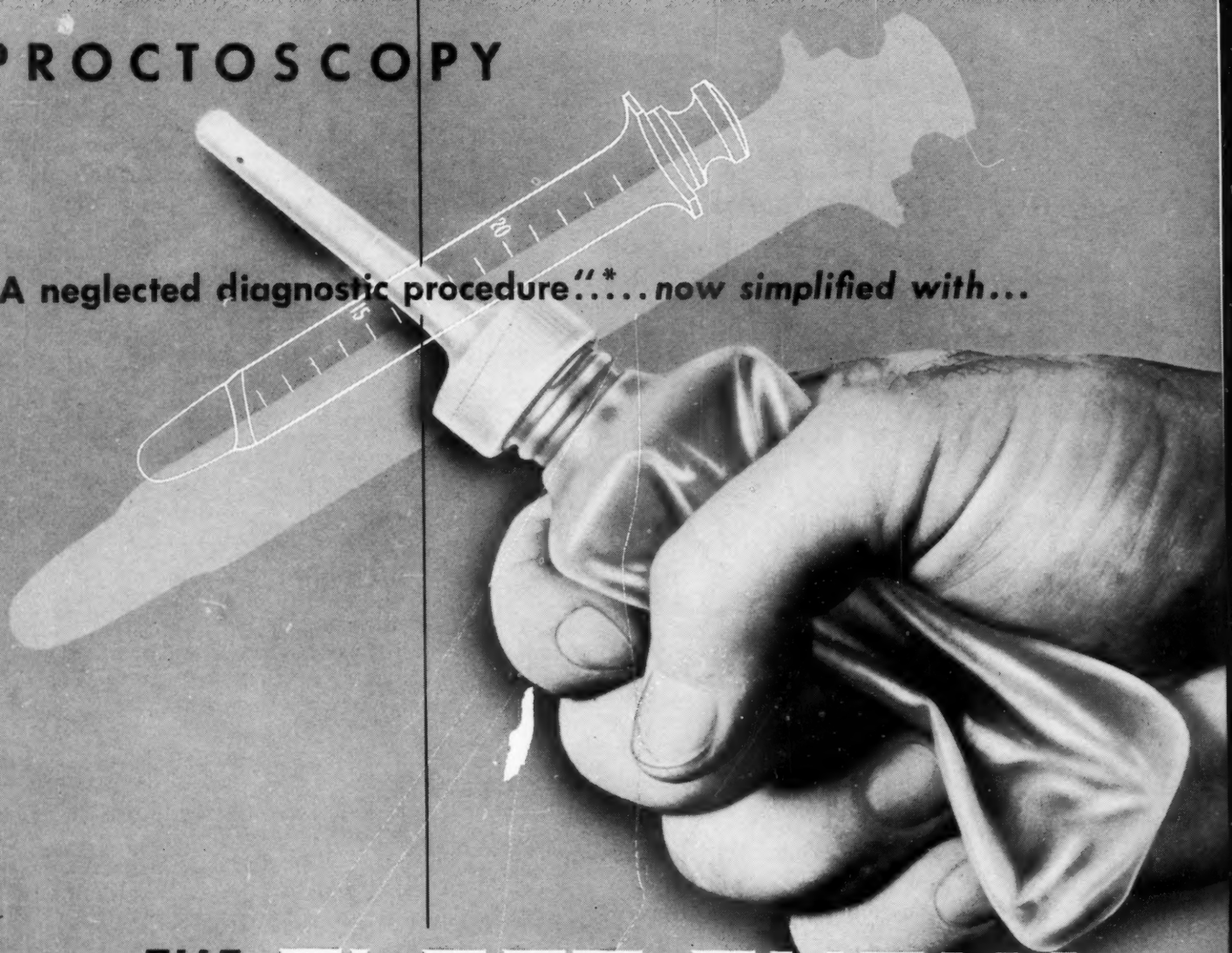

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1. Glenn, F., Evans, J., Hill, M., and McClenahan, J.: Ann. Surg. 140:600, 1954.

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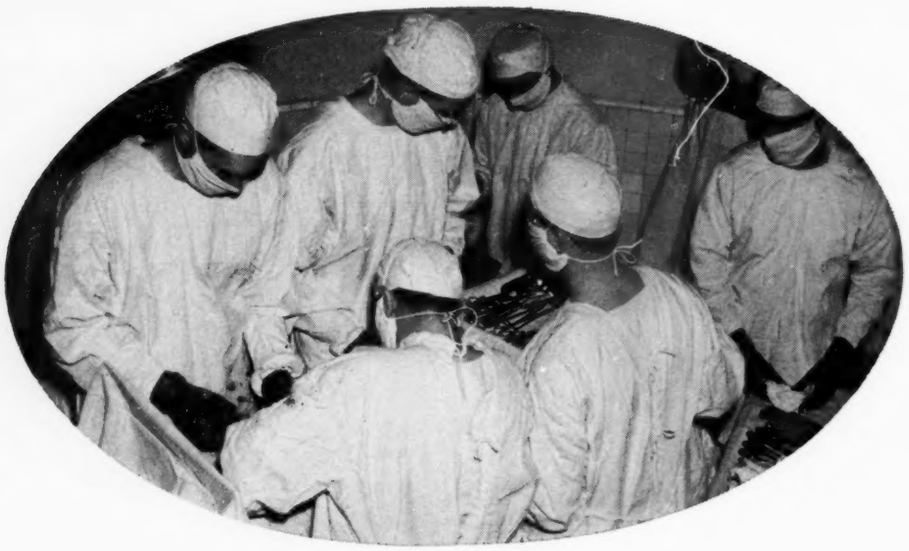

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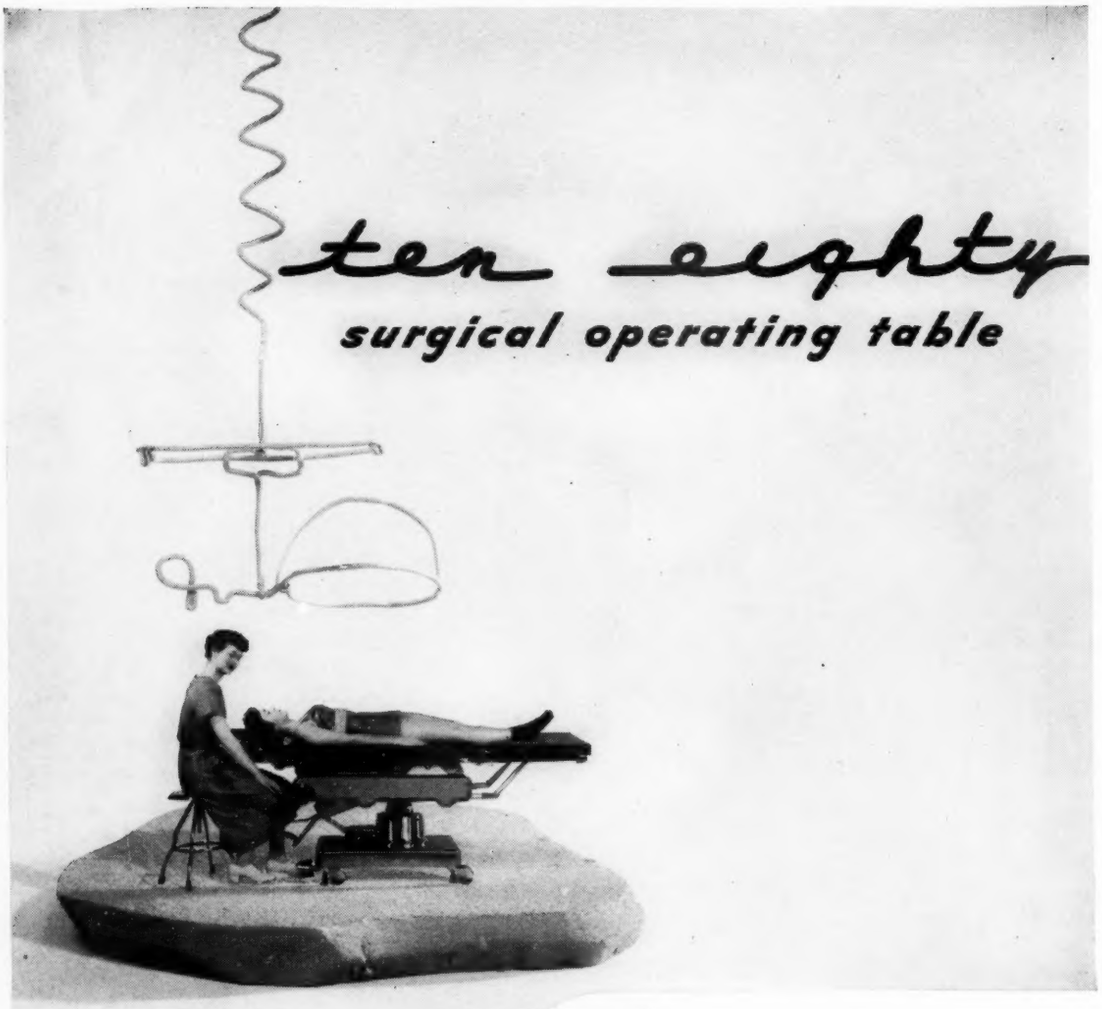

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References: (1) Rosser, J. H., and McCall, R. A.: U.S. Armed Forces M. J. *5*:658, 1954. (2) Kantor, J. L., and Kasich, A. M.: Handbook of Digestive Diseases, ed. 2, St. Louis, The C. V. Mosby Company, 1949, p. 502. (3) Schwimmer, D.; Boyd, L. J., and Rubin, S. H.: Bull. New York M. Coll. *16*:102, 1953. (4) Best, R. R.; Rasmussen, J. A., and Wilson, C. E.: A.M.A. Arch. Surg. *67*:839, 1953.

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Finnerty, F.A., Jr.: Am. J. Med. *17*:629 (Nov.) 1954.

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Livesay, W.R., et al.: J.A.M.A. *155*:1027 (July 17) 1954.

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Lipsett, M.B., et al.: California Med. *81*:412 (Dec.) 1954.

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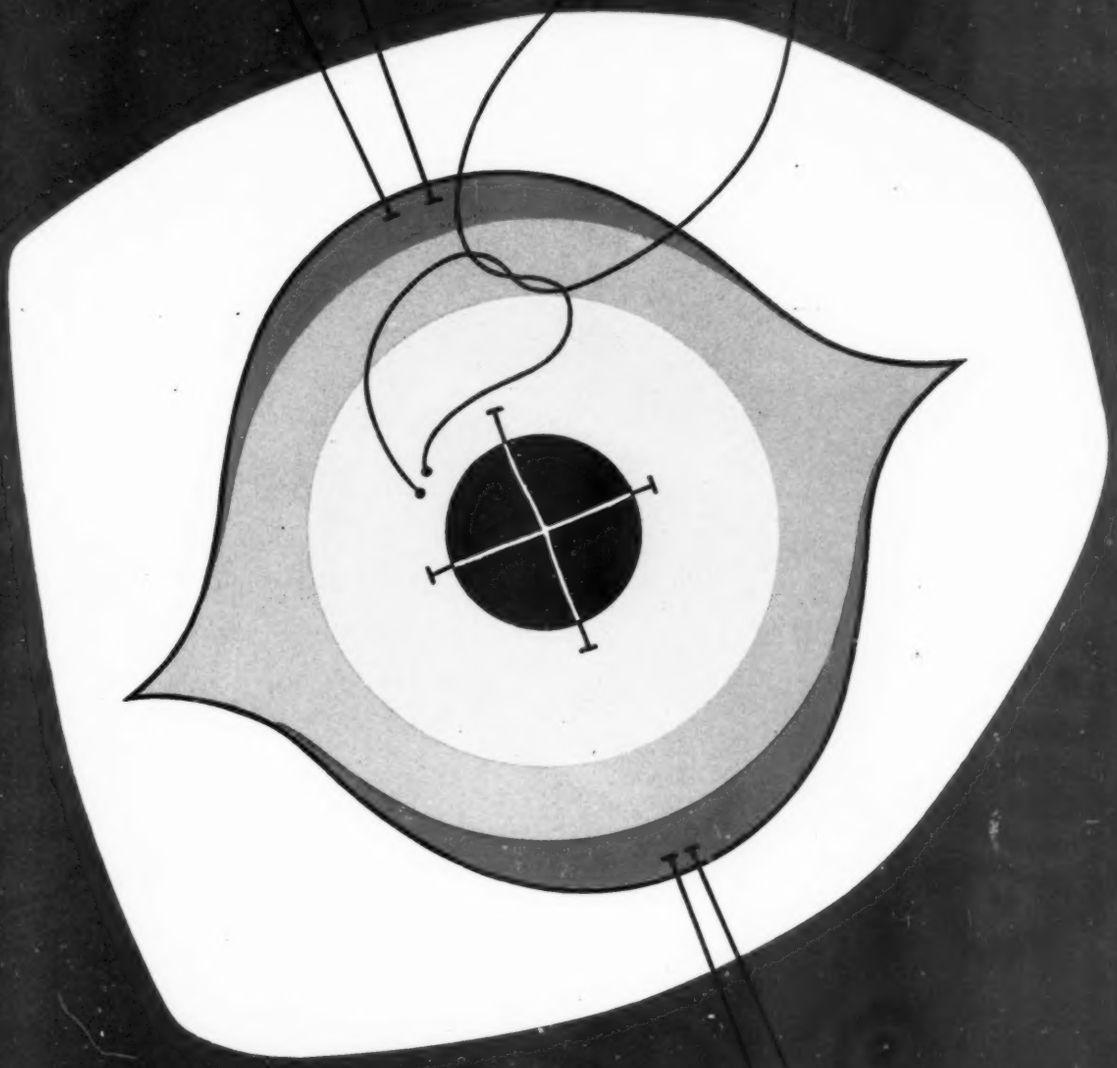
Wilkins, R.W.: Mississippi Doctor *30*:359 (Apr.) 1953.



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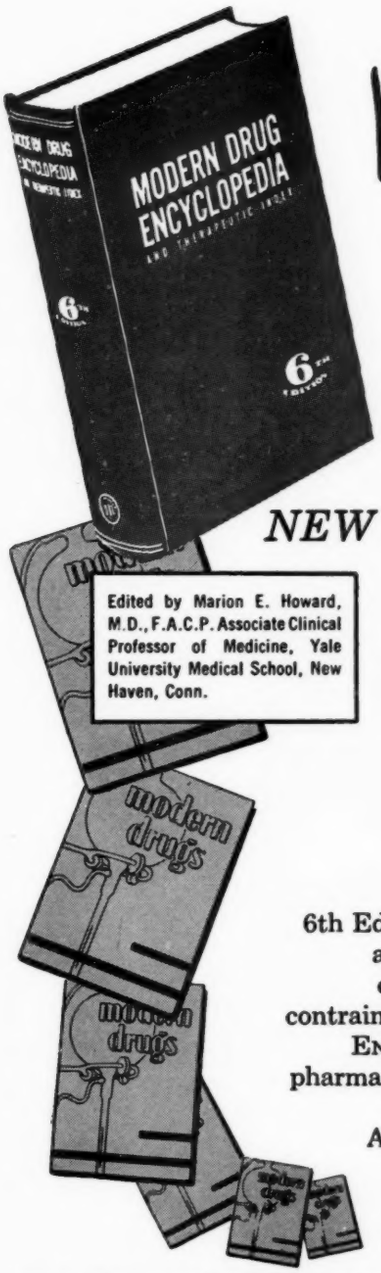

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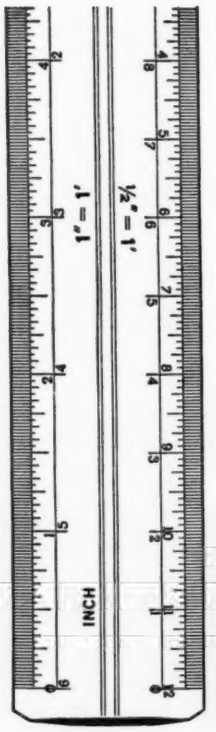

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1 Collette, T.S.: Editorial—False Faith in the Surgeon's Gown and Surgical Drape: Am. J. Surg., 83:125-126, 1952.
2. Propst, H.D.: The Effect of Bactericidal Agents on the Sterility of Surgical Linen; Am. J. Surg. 86:301-308, 1953.
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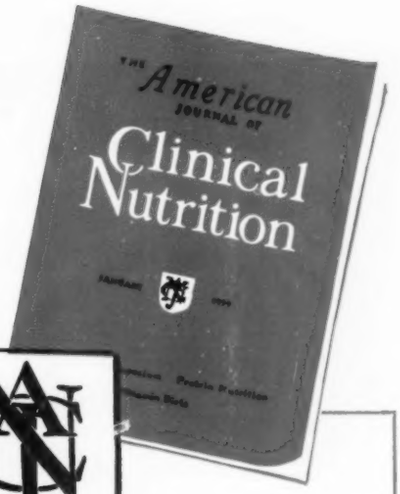

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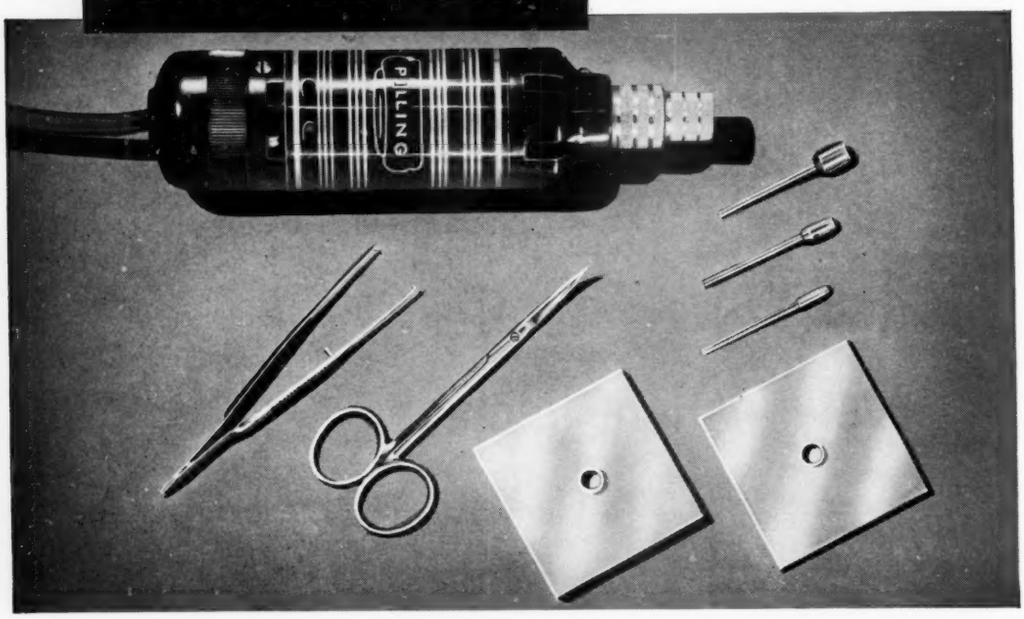

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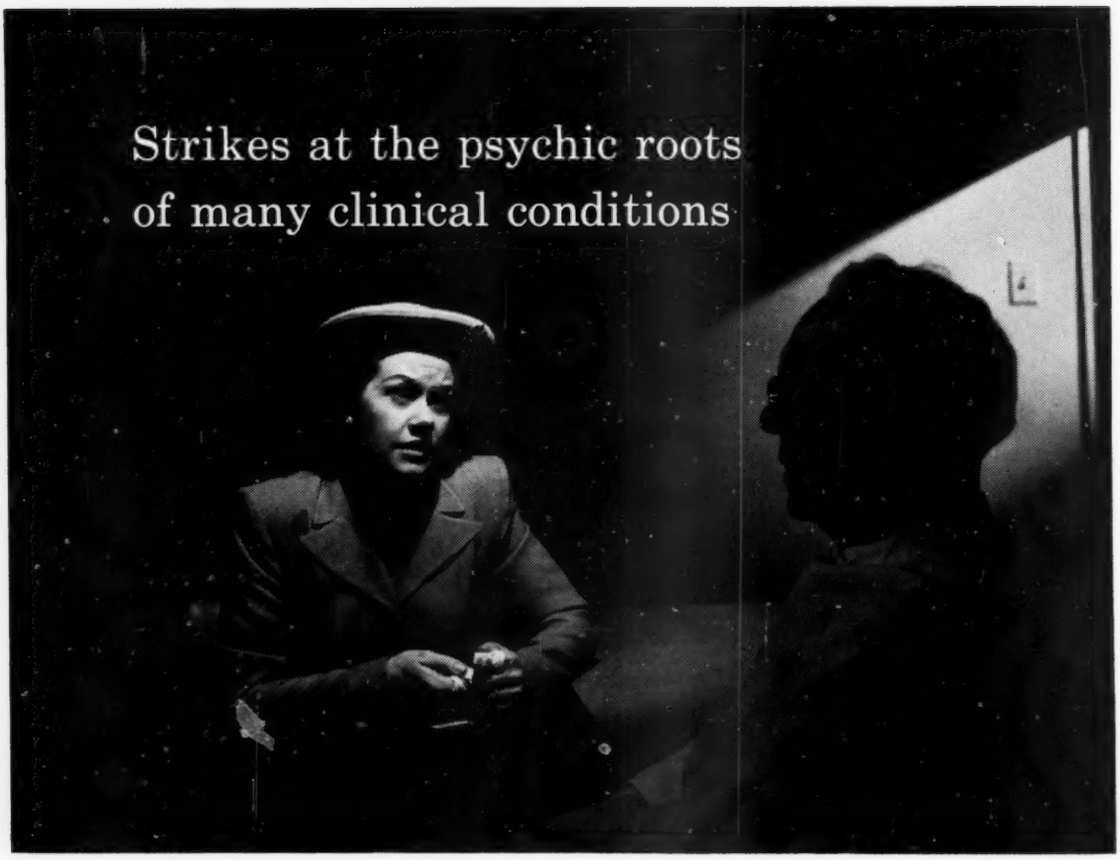

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Editorial

MOTORIST INJURIES

MEDICAL interest in mechanical injuries is being stimulated by the ever increasing number of traffic accidents and their attendant injuries, especially those received by automobile occupants during crash conditions and upsets. This interest, however belated, is most welcome at this time when both human engineering and crash-impact engineering points of view are striving, on an epidemiologic approach to their respective problems, to prevent and/or to moderate traffic accidents and motorist injuries. Valid medical data are essential to the success of both disciplinary projects. Medical groups are asked to recognize these researches and cooperate wherever possible, especially with those who are currently conducting statewide crash-impact field surveys. The latter data are to be used for the purpose of helping to make modern automobiles more crashworthy; in other words to give occupants more protection under crash conditions through more effective safety design. Admittedly, most of this will be based on adequate experimental observations which deal with the how and why of motorist injuries. In the meantime, careful clinical studies can, as they have proved to do in the past, offer considerable supplementary information, to say nothing of their intrinsic common sense value.

During 1954, 123 injured motorists were admitted to the Missouri Methodist hospital and treated by various members of the medical and surgical staffs. Since the prevention of the primary accidents themselves hinges upon driver proficiency, it is to be noted that there were forty-three men and sixteen women drivers in this series of injured people. The decade distribution was as follows: ten patients in the 2nd, fifteen in the 3rd, fifteen in the 4th, eight in the 5th, seven in the 6th, four in the 7th and two in the 8th. The series is small but the implications regarding the need for improved driving among all decades and both sexes is obvious.

The second important point from the standpoint of epidemiology concerns the highway facility or conditions of the external automotive environment. Here, above all else, is to be noted the real lag between automotive engineering progress and highway development. It is only too true that the behavior of the driver en masse (McDonald) must decide how these highways are to be built. A few hints as to present day highway inadequacies are to be seen from the type of accidents as reported in this series: collisions with other vehicles thirty-four (fourteen head-on); roll-overs fourteen; runs off the road five; loss of control two; and collision with fixed object two. It is to be remarked that nineteen individuals were injured in accidents which involved commercial carriers of one kind or another, which points up the narrowness of many of our roads. The mechanism of accident was not recorded in most of the medical records.

The third significant point with regard to the vehicle, under way, is its performance from the standpoint of safety engineering as distin-

guished from safety automotive design. Advances made from this angle (despite the controversial character of some of these) can hardly be disputed. One wonders, of course, at such accident mechanisms as roll-overs, runs off the highway and forcible ejection of people from the car (nine in this series) during crashes and upsets. The phrase, "lost control of the car," is not specific but provocative of thought along these lines. Be that as it may, I find little to criticize from the standpoint of automotive safety engineering of modern automobiles.

Finally, one comes to the factor of most importance, from the standpoint of prevention or moderation of injuries which result from automobile accidents. The basic predisposing factors leading to occupant injuries are force, collapse of structure and human tolerances (local and general) to deceleration impacts. The latter takes into consideration also the relation of occupants to impact areas. The primary force derives from the external automotive environment because of the rapid and ungoverned dissipation of kinetic energy which results from crash deceleration. Because of the geometric relationship to velocity, the foot pounds of energy which are dissipated in crashes of even relatively low velocities come to almost fantastic amounts. However, the manner in which the structure collapses (progressive with absence of peaking is preferred) determines largely how the force will be transmitted to occupant compartment (internal automotive environment). A prerequisite to occupant safety is therefore the maintenance of interior structural integrity.

The forces operating inside the automobile under crash conditions are relative to that of the external environment but act differently because of the smaller deceleration distances through which they act on people (brief duration) and the greater decelerative forces resulting therefrom (hundreds of gravities vs. milliseconds). Some idea of this may be realized from the fact that a 25 pound object going 25 miles per hour when decelerated within 1 inch becomes 1,000 times heavier at the maximum period of stopping (1,000 g). How much kinetic energy can be built up by humans is illustrated by the behavior of Stapp's 175 pound dummy when he is decelerated in the rocket sled from approximately 150 to approximately 75 miles per hour in a space of 9 feet. The dummy rips away from two 1,000 pound straps, smashes through a 1 inch thick board wind screen and hurtles straight down the track to rest 714 feet forward.

Human tolerances to impacts are being established gradually, although the difficulties encountered in attempting to determine the elastic limits of the body as a whole as well as its component parts can well be imagined due to the enormous variables present. From the crash standpoint, not the magnitudes but the sources (De Haven) (not yet clearly defined) and duration of the forces are important. Furthermore, the distribution of the force application is significant since the body better tolerates pressure over a larger area of the body than it does over a smaller area. Magnitude of forces is therefore lessened through further decelerative distances (or over longer periods of time). It has been supposed on clinical grounds that the seating of persons in the car largely determined the frequency and severity of injuries received. Apparently, present high speeds are leveling off the lethal potentialities of the different seating areas. This relationship could be established in 102 cases in this series. Among sixty-one drivers there were thirty-eight (62 per cent) minor to moderate injuries, twenty-one (34 per cent) severe injuries, and two (4 per cent) dangerous injuries (no mortality). Among thirty-one front seat passengers there were thirteen (42 per cent) minor to moderate injuries, thirteen (42 per cent) severe injuries, and five (16 per cent) dangerous injuries (with one death, 3 per cent mortality). Among ten rear seat passengers there were eight (80 per cent) minor to moderate injuries, one (10 per cent) severe injury, and one (10 per cent) dangerous injury (one death, 10 per cent mortality).

A few general statistics are of interest. Fifty-three patients of this series did not have any fractures (46 per cent); seventy (54 per cent) did have fractures. Of the non-fracture group, thirteen (25 per cent) had single injuries and forty (75 per cent) had multiple injuries. Of the fracture group, sixteen (23 per cent) had single injuries and fifty-four (77 per cent) had multiple injuries. Of the entire series, 23 per cent had single injuries and 77 per cent had multiple injuries. Among the non-fracture group, cerebral concussion was noted in three people with single injuries and in nineteen with multiple injuries. Cerebral concussion was stated to be present among the fracture group in one of those with single injuries and in ten with multiple injuries. Of the entire

series, cerebral concussion was noted in 27 per cent. On the other hand, shock was noted in only two cases of the non-fracture group (mild) as against twelve in the fracture group. On the whole, shock was said to have been present in 11 per cent of these persons.

Some idea of body tolerance to crash impacts is to be noted from an analysis of the body areas involved in injury in this series. Twenty-one or 17 per cent of these people had, in addition to injuries which could be more specifically classified, widely distributed multiple injuries, chiefly contusions and abrasions. More specifically, seventy-eight persons (63 per cent) showed involvement of the head and face; seventy-two (59 per cent) received injuries to the extremities; forty-three (35 per cent) had injuries to the trunk and pelvis (including a small number of neck injuries); 42 people (35 per cent) sustained injuries to the chest; and only five persons (4 per cent) had injuries to the abdomen. These figures compare closely with those of larger comparable series. The following areas were involved in fractures in this series: extremities, thirty-five persons; thorax, thirty-three; face, seventeen; spine, eleven; pelvis, five; and skull, five.

The clinical life history of the motorist involves considerations of mortality, morbidity, predisposing causes and prophylaxis. The basic responsibility of medical groups must remain that of aggressive treatment of any and all kinds of injuries. The large number of victims sustaining fractures of the extremities focuses attention upon the urgent need for improved first aid and especially splinting of these injured bones. Lay groups must be indoctrinated with simple practical methods of splinting. By the same token, the same principles must be adhered to after the patient reaches the hospital. The relatively large number of shock patients indicates the urgency of emergency treatment in the hospital. As has been stated, these people are either getting better or getting worse from the time of injury, and brook no delay in active and specific treatment. Finally, the complexity of the severely injured and especially the dangerously injured persons will tax the ingenuity and stamina of the most conscientious medical and surgical attendants. Equally true is the fact that no other type of case, brought through to a successful result, brings any more satisfaction than do these trying and challenging ones.

However important and difficult diagnosis and treatment may be, the prevention of these injuries is even more important. This may be accomplished in two ways: (1) prevent the accidents in the first place, or (2) moderate the injuries which result from these accidents. Medical groups can help by focusing attention upon both accident and injury prevention to the public. A positive attitude has not yet been achieved among the latter in this regard. A positive approach to all of these problems should derive from the realization that this situation, from the standpoints of treatment and prevention, could prove to be a training ground for possible catastrophic casualties to come, whether these be from atomic or natural sources engendered by war, pestilence or storm conditions. However that may be, medical groups are expected to take a very active leadership along these lines.

The more obvious participation of medicine in research, etc., has not been mentioned. Much of this is in progress. The prophylactic measures having to do with engineering and design components have not been mentioned because these, likewise, are being taken care of by competent research authority. Investigations are now in progress with regard to injury potentials of automobiles, which promise to alleviate the plight of the motorist who finds himself in imminent danger of crash deceleration or upset.

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SCIENTIFIC PAPERS

Intravenous Cholangiography

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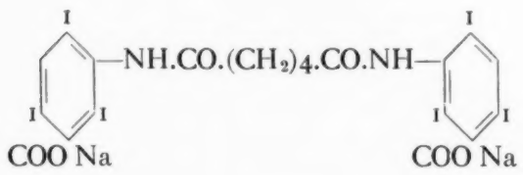
THE use of telepaque® in oral cholangiography has made it possible to visualize the biliary ducts in 78.75 per cent of cases in which there has been successful visualization of the gallbladder.[1] Although this percentage can be increased appreciably by taking roentgenograms at shorter intervals or by repeating the cholecystography the following day or some days afterward, it is not possible successfully to visualize the biliary ducts when the gallbladder is functionally inactive (fails to visualize) or when the patient has had cholecystectomy.

The number of gallbladders which are found roentgenologically non-functioning is considerable. Before the substance known as biligrafin* (cholografin®) was discovered, it had not been possible to visualize the biliary ducts in patients who had had cholecystectomy. This substance has been made available to fill this gap in roentgenologic diagnosis, initiating an era which may properly be called the "era of intravenous cholangiography."

Cholografin is the di-sodium salt N,N-adipyl-bis (3-amino-2,4,6,-triiodo) benzoate solution, whose empiric formula is $C_{20}H_{12}O_6N_2I_6Na_2$, which has the following structural formula:



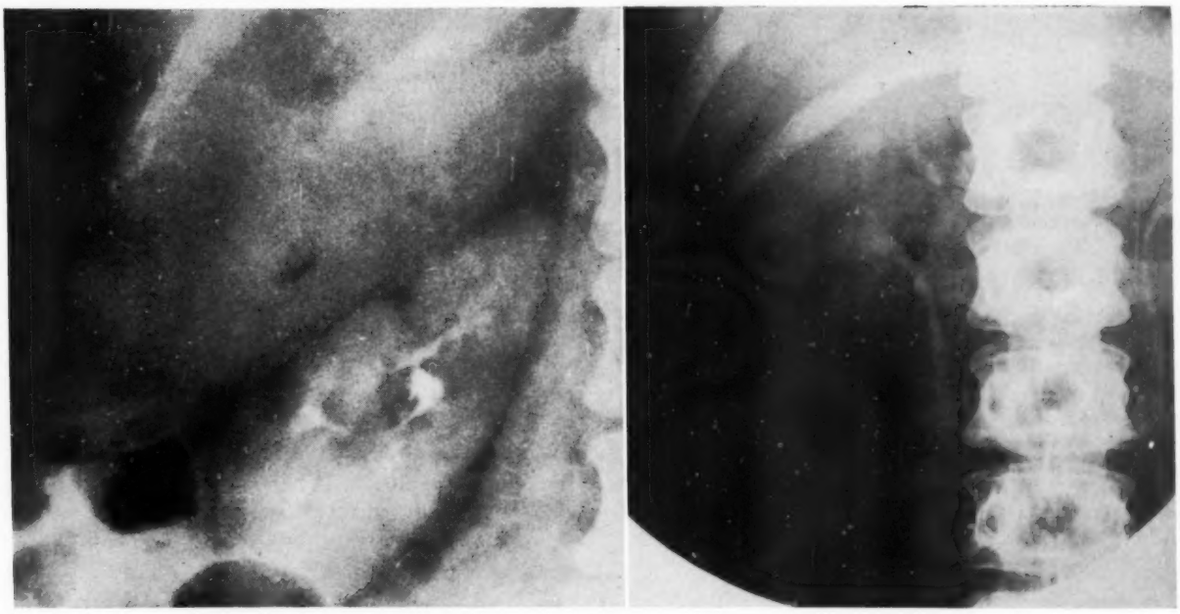
The new preparation has an iodine content of 64.32 per cent, with 6 atoms of iodine in each molecule; it is very soluble in water. It is obtained in the form of a crystalline powder and may be found commercially in clear isotonic 20 per cent solution. It is employed by intravenous injection in doses of 4 to 8 gm.

Cholografin, as contrasted with telepaque, does not exhibit an enterohepatic cycle. The substance reaches the liver by the blood stream and acquires a pronounced concentration in the biliary ducts before reaching the gallbladder. This difference between cholografin and other media employed in cholecystography is fundamental. The ordinary drugs previously employed reach the gallbladder in very dilute form, and therefore it is necessary for the gallbladder to be functionally sound and exercise its capacity of concentration in order that the gallbladder may be visualized on the roentgenograms. The gallbladder which is visualized well in cholecystography when employing telepaque, teridax® or priodax® is an organ with healthy walls (from the roentgenologic viewpoint), for otherwise there would not be concentration of the opaque substance nor a shadow of the gallbladder. On the other hand, the visibility of the gallbladder with cholografin is not dependent upon the state of the gallbladder walls; it is sufficient that this organ be permeable for it to become roentgenologically visible.

Visibility of the biliary ducts in oral cholangiography is not achieved except during the periods of active gallbladder evacuation. However, since in intravenous cholangiography the ducts become visible before the opaque substance reaches the gallbladder, these ducts may become recognizable in cholecystectomized patients or in cases of obstruction of the cystic duct, atrophic gallbladders or gallbladders filled with stones.

In accordance with the studies done thus far, beginning with the first communications on this material made by Frommhold[2–4] on May

* Biligrafin, A. G. Schering, West Berlin, Germany. (Cholografin, Squibb Institute for Medical Research, New York, N. Y.)



1 2

FIG. 1. Renal elimination of cholografin. Visualization of the right renal calyces ten minutes after the injections.

FIG. 2. Elimination of cholografin by the urinary tract. Bilateral visualization of pelves and ureters; also faint visualization of normal cystic and common ducts. (See Figure 14, same patient.)

16, 1953, cholografin is very well tolerated by patients. We therefore resolved to go ahead with some preliminary studies on patients in our private practice whenever we considered this method of examination indicated. Our results were presented at the Third Colombian Radiological Conference in November, 1953.[5]

The results obtained with cholografin have been so satisfactory that it has seemed to us desirable to publicize the results as soon as possible.

The only contraindications, so far as known, are serious disturbances of hepatic function, Basedow's disease and cases of hypersensitivity to iodine. Regarding the latter, we consider that cholografin presents the same problem as all other iodized substances used routinely for urography, arteriography and angiocardiography, and for that reason it is necessary before the examination to make some test which may indicate the presence or absence of hypersensitivity to iodized substances. The ocular and the intradermal reactions have not been used by us routinely in urography and arteriography because we consider it sufficient to introduce the first 3 cc. of the contrast substance and then wait a few minutes to see if the patient tolerates the injection without any significant allergic phenomena. In the same way we have proceeded with cholografin.

A percentage of cholografin is eliminated by the urinary apparatus. Since this percentage increases in patients with hepatic insufficiency and since in some patients who suffer from non-obstructive jaundice the iodized substance was well tolerated, it has not seemed that there was a definite contraindication offered by serious disturbance of hepatic function. In twenty-three of the sixty-three cases examined, in the films exposed five and ten minutes after the injection it was possible to observe visualization of the renal pelves and calyces by the prompt excretion of the opaque substance. In fifteen of these cases it was possible afterward to obtain good visualization of the gallbladder or of the biliary ducts, and to confirm the elimination of a part of the opaque substance by the kidneys. (Figs. 1 and 2.)

Patients' tolerance of cholografin may be briefly summarized as follows:

Patients examined with cholografin	63
Injection well tolerated	36
Slight nausea at end of injection	14
Vomiting	5
Discrete urticaria	4
Pronounced urticaria (1 with edema of lips and eyelids)	2
Attacks of sneezing on ending the injection	2

FIG. 3. Dilated common duct containing five stones. Gallbladder blocked by cystic duct stone; studied with cholografin.

In addition to the foregoing there were four patients in whom, along with the symptoms indicated, there was complaint of flushing of the face.

In eight of our patients there was failure to visualize the hepatobiliary system. In four of them no explanation could be found for this failure to visualize, but among the other four there were two who presented non-obstructive icterus and the other two had suffered severe colic of the biliary type in the days immediately preceding the roentgen examination. It was therefore thought that poor liver function was responsible for this failure of visualization. One of the observations is very interesting because the cholangiography made during a painful crisis did not show any intraductal shadows; but on repeating the examination fifteen days later when the patient had returned to his customary program, the dilated common duct containing five calculi was clearly demonstrated. (Fig. 3.) The gallbladder was not visualized because a stone was encapsulated in the cystic duct. At operation these stones were found in the common duct, one in the cystic duct and other large stones in the interior of the gallbladder.

We desired also to submit patients in advance to the different laboratory tests which could give us information concerning hepatic function although up to the present we have not been convinced of their utility. This is because in one of the cases with normal laboratory tests no roentgenologic shadow was obtained, and in another with tests indicating poor function of the liver, the examination when repeated showed that these tests had returned to normal, still without securing roentgenologic visualization.

Both oral and intravenous cholecystography give similar results when the gallbladder has normal concentrating function. The case shown in Figures 4 and 5 is that of a patient with excellent concentrating function of the gallbladder and small cholesterol stones in the gallbladder, examined roentgenologically by two different tests, with an interval of three days. As may be seen in these roentgenograms, the shadows obtained after complete filling are similar as far as concerns the concentration of the dye in the gallbladder. With telepaque and in the vertical position, the horizontal line is seen representing clearly the cholesterol stones. On the other hand, in intravenous cholangiography the more dense bile, which has reached the gallbladder along with the contrast medium, pushes downward the bile which was already in this organ and does not permit as clear depiction of the shadows of the stones as in the study made with telepaque. At the same time it can be said that when the gallbladder begins to fill with cholografin, the shadow is not homogeneous because of the difference in density between the bile which was already in the gallbladder and that which enters the gallbladder carrying with it the cholografin. (Figs. 6 and 7.)

However, in reality it may be said that when the gallbladder has normal contracting function, the results are essentially equal with the two procedures. It is much easier to give the patient a few tablets on the evening before examination, to take roentgenograms of the completely filled gallbladder the following day and then to repeat the study from fifteen to twenty minutes after the fatty meal than it is to give an intravenous injection of 20 cc. and hold the patient for two hours in the office while subsequent roentgenograms are being made. We therefore consider that as a routine method the use of oral cholecystography should continue. Cholografin is necessary only in cases in which the gallbladder shadow fails to appear by cholecystography and in those cholecyst-

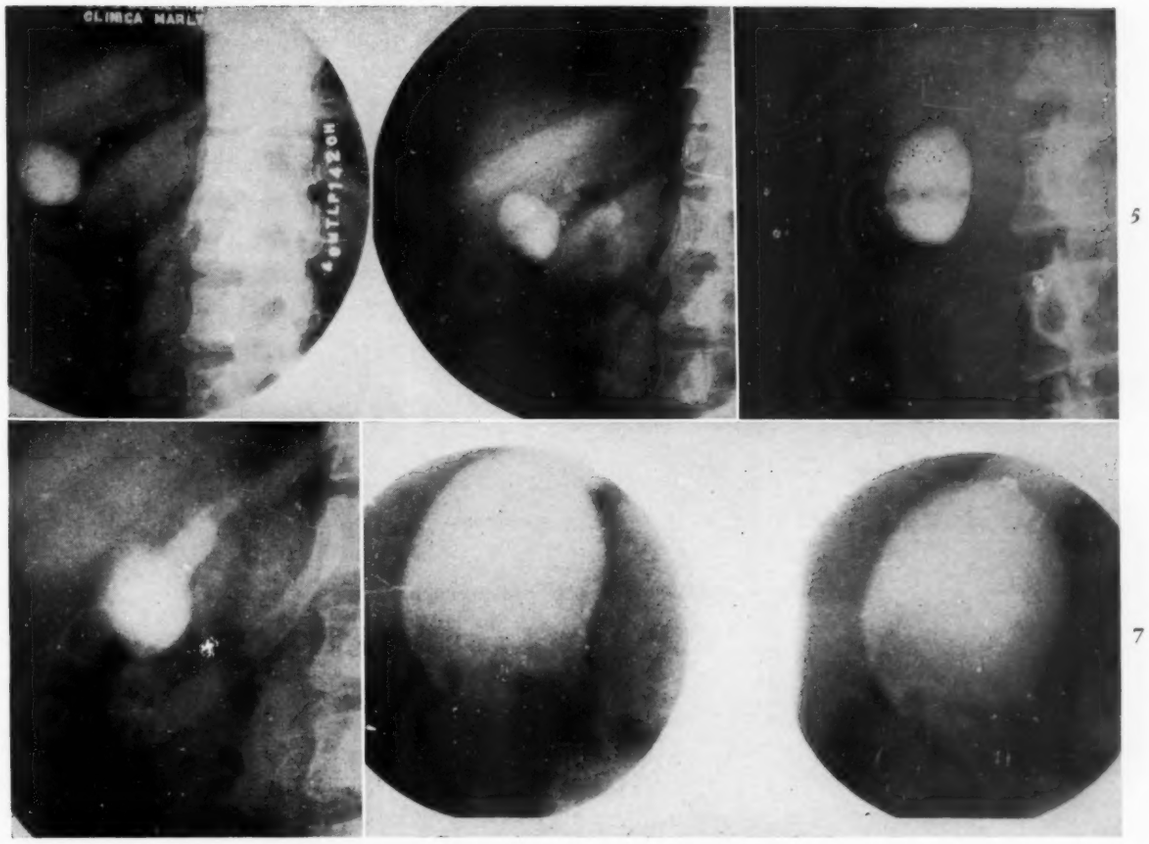


FIG. 4. Telepaque. Small vesicular stones, normal ducts, ventral decubitus.

FIG. 5. Telepaque. Same patient as in Figure 4, in the erect position. Gallbladder stones are well shown.

FIG. 6. Cholografin. Same patient; gallbladder shadow not yet homogeneous at thirty minutes after injection.

FIG. 7. Cholografin. Same patient, in the erect position. The gallstones appear in the fundus of the gallbladder and are not as clearly shown as with telepaque.

ectomized patients in whom one cannot obtain visualization of the ducts with telepaque.

In twelve of the sixty-three patients examined the gallbladder and the biliary ducts were functionally and morphologically normal. In eight of these the study was made by both oral and intravenous methods, with similar results, and in the other four examination was done with cholografin without previous cholecystography. In two, small gallbladder calculi were found.

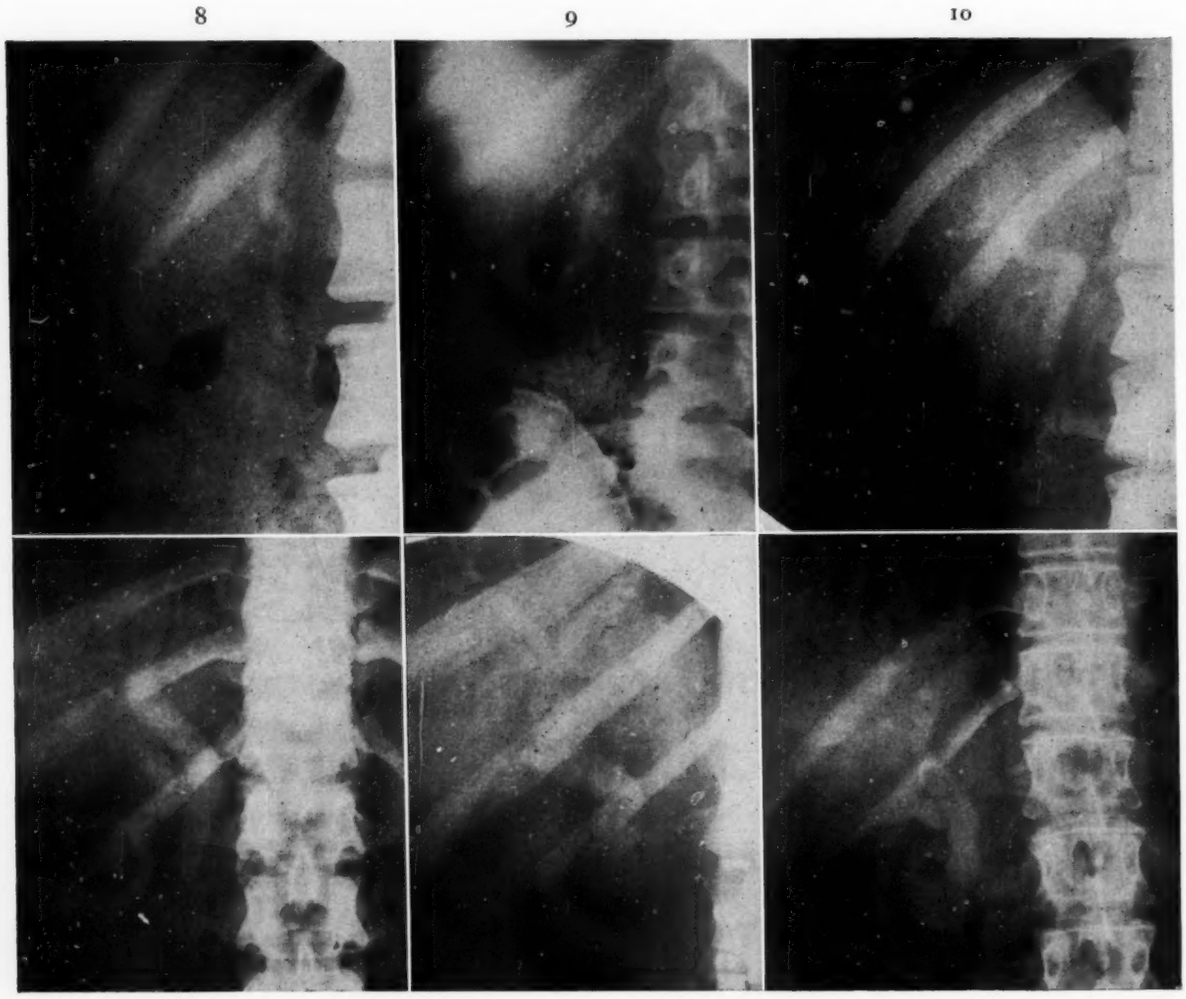
Of the fifty-one patients remaining, eighteen had been cholecystectomized. The results in this group were as follows:

Common and hepatic ducts normal (Figs. 8 and 9)..... 4
Common and hepatic ducts slightly dilated because of moderate odditis (Fig. 10).... 4
Common and hepatic ducts dilated by marked odditis (Fig. 11)..... 2
Common and hepatic ducts with calculi (5 of the common duct and 1 of the trunk of the hepatic duct) (Figs. 12 and 13)..... 6
Biliary ducts not visualized..... 2

Furthermore there were three cases in which there was visualization of the trunk of the cystic duct (Fig. 13), one of which may be considered as a reconstruction of a rudimentary gallbladder.

In the two cases in which there was no visualization at all one had had division of the common duct at the time of the cholecystectomy; and although it had been sutured afterward, this canal was connected with the skin by a fistula through which bile was draining.

The other thirty-three patients had not been



8 9 10 11 12 13

FIG. 8. Cholografin. Cholecystectomized patient; normal ducts.

FIG. 9. Cholografin. Cholecystectomized patient; normal ducts; opaque substance in the duodenum.

FIG. 10. Cholografin. Cholecystectomized patient; discrete odditis.

FIG. 11. Cholografin. Cholecystectomized patient; marked odditis. There is a stone in lower portion of common duct.

FIG. 12. Cholografin. Cholecystectomized patient; marked dilatation of common duct and trunk of hepatic, containing four large stones.

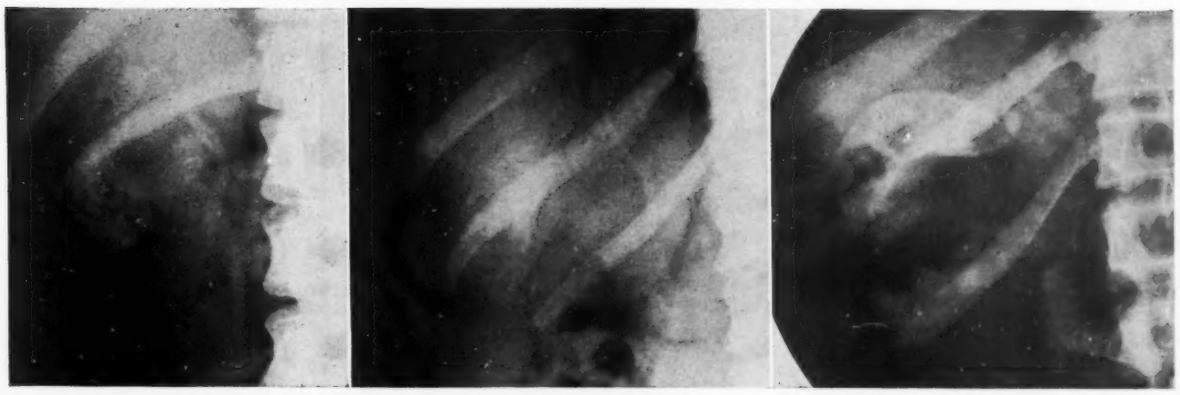
FIG. 13. Cholografin. Cholecystectomized patient; stone in lower portion of hepatic duct. Rudimentary reconstruction of gallbladder in stump of cystic duct.

operated upon and oral cholecystography with a double dose of telepaque had presented no vesicular shadows and no calculi opaque to the x-rays.

In fifteen there was visualization of the ducts as well as of the gallbladder. In eleven the ducts were visualized but not the gallbladder.

In seven there was no visualization either of the ducts or of the gallbladder. In these seven there were six with pronounced icterus: In four it was non-obstructive, with no history of colic; two had colic, apparently biliary, but these patients were lost sight of and no follow-up was possible. The last of these seven cases showed at surgery two large cylindric cholesterol calculi originating in the common duct, with the cystic duct extremely narrow and the gallbladder without stones and full of stagnant bile.

Gallbladder stones were found in all of the fifteen cases in which the ducts and gallbladder were visualized. Eleven patients had normal

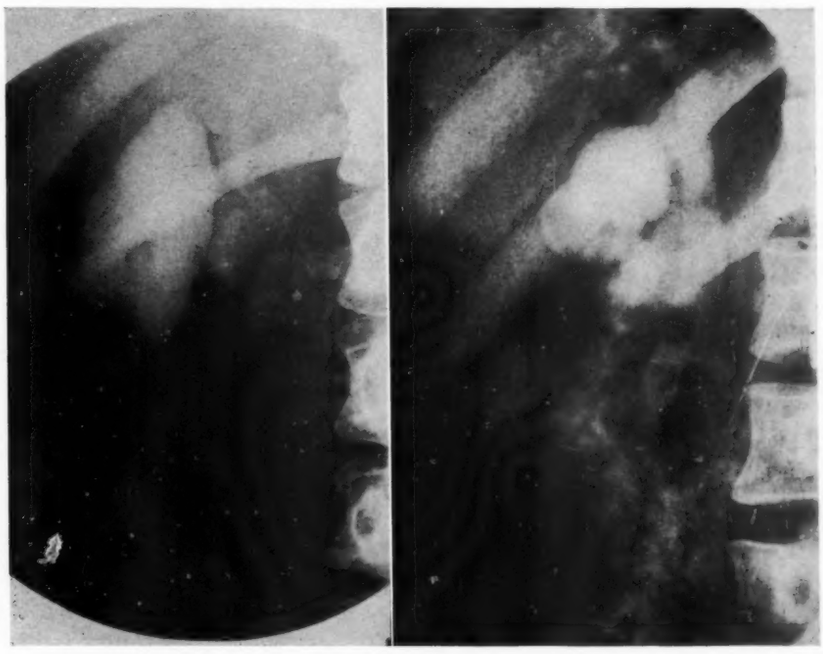


14 15 16

FIG. 14. Cholografin. Gallbladder stones; normal ducts. Renal elimination. Failure of visualization with telepaque.

FIG. 15. Cholografin. Gallbladder stones; normal ducts. Failure of visualization with telepaque. Gallbladder wall is damaged.

FIG. 16. Cholografin. Gallbladder filled with stones; normal ducts. Wall of gallbladder pathologic. No visualization with telepaque.



17 18

FIG. 17. Cholografin. Gallbladder stones; discrete odditis without intraductal calculi.

FIG. 18. Cholografin. Stones in gallbladder and common duct, with marked ductal dilatation.

ducts (Figs. 14, 15, and 16), four had dilation of the common duct due to odditis (Fig. 17) and two had common duct stones. (Figs. 18, 19 and 20.)

In the eleven cases in which the ducts alone were visualized but not the gallbladder, five patients had odditis, five had normal ducts and one had a calculus in the trunk of the hepatic duct. The failure of visualization in these cases should be due always to some physical factor which does not permit the entry of the opaque substance into the gallbladder, whether the cause is complete filling with stones (sometimes very small stones) or, as has occurred most

FIG. 19. Cholografin. Biliary sand in the gallbladder and tiny gallstones in the sphincter of Oddi, with relative dilatation of the common duct.

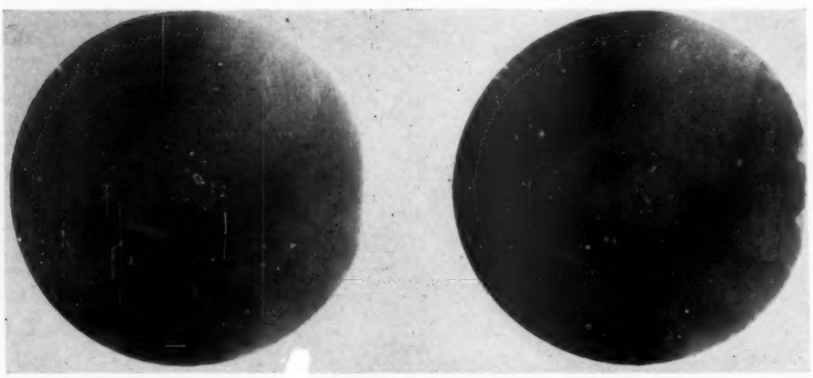


FIG. 20. Cholografin. Same case as Figure 19; erect position showing very well the small stones in the gall bladder.

frequently in our experience, a large stone trapped in the cystic duct or in the superior portion of the infundibulum.

Before the advent of telepaque there were occasional cases of visualization of the biliary ducts. Now, however, the ducts are almost always visualized with routine oral cholecystography provided that the gallbladder has normal concentrating function. In non-visualizing gallbladders and in cholecystectomized patients we have succeeded in visualizing the gallbladder or common duct with intravenous cholangiography in a very large number of cases.

As already stated, in our work on oral cholangiography presented by one of us at the conference on gastroenterology held in Cali, Colombia,[1] the era of oral cholangiography was initiated with the discovery of telepaque, and the utilization of cholografin in intravenous cholangiography is the first step in a new era toward the study of the biliary ducts in those patients in whom the oral procedure does not result in gallbladder visualization. It is our opinion that in patients with normally functioning gallbladder in whom the value of both procedures is about equal it is easier and simpler to employ oral cholangiography; however, in those cases in which cholecystography has been positive, and in cholecystectomized patients, the use of cholografin permits visualization of the gallbladder or biliary ducts, an accomplishment which previously has not been possible.

In accordance with the foregoing considerations, it is now within our power to visualize the biliary ducts and the gallbladder in the major portion of patients examined. This gives

us assurance, as we have already said, that with the improvements being made daily in technic and possibly with the introduction of new substances, we shall shortly succeed in perfecting cholangiographic studies in the same degree as cholecystography has been perfected.

CONCLUSIONS

Since cholecystography and oral cholangiography do not permit visualization of the biliary ducts when the gallbladder fails to visualize or when the patient has been cholecystectomized, it is recommended in these patients to employ intravenous cholangiography with cholografin routinely.

It is not considered convenient to replace the oral procedure by the intravenous method except in the cases just indicated, since cholecystography is very easily carried out and gives as good results as intravenous cholangiography provided that the gallbladder is permeable and has normal contracting function.

In sixty-three cases examined by the intravenous procedure it has been demonstrated that cholografin is well tolerated by the patient. In 85.71 per cent of cases success has been achieved in making an exact diagnosis of the state of the biliary ducts. On the other hand, gallbladder visualization has been achieved in 45.45 per cent of patients whose gallbladders were functionally nonvisualized in cholecystography.

Intravenous cholangiography is of great value not only because it affords knowledge of the condition of the biliary ducts before cholecystectomy but also because of the information which it furnishes in cholecystectomized individuals. At the present time the only means of roentgen demonstration of odditis, dilation and intraductal stones in cholecystectomized patients is intravenous cholangiography.

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Complications from Resection of the Colon

AN EVALUATION OF COMPLEMENTARY CECOSTOMY

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ALTHOUGH there is general agreement that some type of proximal stoma is required in the presence of complete large bowel obstruction,[2,3,5] there has been a trend in recent years away from decompression by complementary cecostomy or colostomy in the management of non-obstructive lesions of the colon. This transition, which is attributable in large part to the widespread use of intestinal antiseptics, gastric suction and antibiotics, is illustrated by several articles which have appeared in the literature in the past few years.

In reviewing thirty-four consecutive cases of primary resection of the colon for carcinoma, McNealy and Lands[1] expressed the opinion that not only are complementary vents unnecessary with the use of continuous suction, but also they add the burden of possible wound infection or further operation.

Gunkler and Pearse,[2] in discussing a series of cases of resection of the colon for carcinoma, stated that a proximal vent is not necessary unless obstruction is present. In support of this conclusion a mortality of 6.7 per cent was reported for 163 patients with no obstruction treated between 1938 and 1947 in whom no proximal vent was established.

Rosemond et al.[4] analyzed the complications encountered in a series of eighty-three resections of the colon and concluded that only when trouble develops at the suture line should a proximal vent be used, in which case the decompressive operation could be performed as a therapeutic rather than a prophylactic measure.

In his survey of a group of leading general surgeons and proctologists Graham[3] found that 30 per cent employed surgical decompression when resecting lesions of the left colon.

The present review of cases was undertaken to determine whether complementary cecostomy may still offer certain advantages in the operative treatment of non-obstructive lesions of the colon, and if so, under what conditions this procedure may be indicated. For purposes of our study, the period after 1944 was selected for analysis since penicillin and other antibiotics have been in general use subsequent to that date.

TABLE I

RESECTION OF COLON WITH PRIMARY COLON-TO-COLON ANASTOMOSIS (EXCLUDING RESECTIONS OF CECUM AND ASCENDING COLON)

Non-obstructive Lesions	
No proximal stoma	159
Complementary cecostomy	67
Total cases	226

During the eight-year period from January 1, 1945, to January 1, 1953, 226 resections of the colon were performed as elective procedures for non-obstructive lesions at the University of California Hospital. (Table I.) Excluded from this total were resections involving lesions of the cecum and the ascending colon, since cecostomies could not be performed in such cases.

The lesions involved were of various types, but the majority of the resections were undertaken for carcinoma or an inflammatory disease, usually diverticulitis. (Table II.) In approximately 75 per cent of the cases the site of the lesion was the sigmoid colon or the rectum, as indicated in Table III.

Of these 226 resections, the closed or aseptic type of anastomosis was used in 161 cases, whereas the open method was employed in sixty-five. (Table IV.) No over-all comparison of the two methods has been attempted, but the type of anastomosis is indicated in analyzing those cases in which complications arose. In most instances an end-to-end anastomosis was performed.

A complementary cecostomy was performed in sixty-seven of the 226 resections, i.e., the cecostomy was established at the time of definitive operation. In every instance the procedure was of the "tube" type with fixation of a large catheter into the cecum; the cecal wall was sutured to the peritoneum but not to the skin. In the remaining 159 cases in which no decompressive stoma was used continuous gastric suction was applied. There were no complementary transverse colostomies in our series.

TABLE II
TYPE OF LESION

Lesion	No Stoma	Cecostomy
Carcinoma, primary	105	36
Carcinoma, other	4	5
Inflammatory disease	23	5
Radiation reaction	5	2
Hirschsprung's disease	2	1
Redundant colon	1	1
Previous colostomy	3	6
Polyps	8	4
Stricture	1	3
Fistula	3	3
Prolapse of rectum	3	0
Endometriosis	1	0
Gangrene (thrombosis of inferior mesenteric artery)	0	1
Total	159	67

TABLE III
SITE OF RESECTION OF COLON

Site	No Stoma	Cecostomy
Hepatic flexure	1	0
Transverse colon	24	11
Splenic flexure	4	1
Descending colon	2	4
Sigmoid colon	79	32
Rectosigmoid colon and rectum	36	17
Left colon (splenic flexure, descending and sigmoid)	13	2
Total	159	67

RESULTS

The operative mortality for the 159 cases in which no proximal vent was established was 3.1 per cent. (Table v.) Four of the five deaths in this group were associated with peritonitis; one death resulted from cardiac arrest.

Of the sixty-seven cases in which cecostomies were performed, there were two deaths or a mortality rate of 3.0 per cent. Neither death was attributable to peritonitis; one patient died of coronary occlusion and the other of shock.

TABLE IV
METHOD OF ANASTOMOSIS

Anastomosis	No Stoma	Cecostomy
End-to-end	152	59
End-to-side	4	2
Side-to-side	3	6
Total	159	67
Open	42	23
Closed	117	44
Total	159	67

TABLE V
MORTALITY

Cause of Death	No Stoma (159 cases)		Cecostomy (67 cases)	
	No.	%	No.	%
Peritonitis	4	2.5	0	...
Coronary occlusion	0	...	1	1.5
Shock	0	...	1	1.5
Cardiac arrest	1	0.6	0	...
Total	5	3.1	2	3.0

Complications resulting from the operative procedure are tabulated in Table VI. Most significant among the group without decompression were the four fatal cases of peritonitis. In addition there were three instances of intra-abdominal abscess and three of fecal fistula. Three other patients required secondary operations because of stenosis at the suture line.

In the cecostomy group there were no cases of peritonitis; however, one instance of pelvic abscess and two of fecal fistula were observed.

Five of the cecostomies persisted as fecal fistulas and required secondary closure. In four cases postoperative small bowel obstruction occurred. In none of these was the cecostomy responsible for the obstruction, but in one patient the loops of intestine were adherent to the region of colonic anastomosis. Obstruction of the colon from stenosis at the suture line was not encountered in the cecostomy group.

TABLE VI
COMPLICATIONS SECONDARY TO OPERATIVE PROCEDURE

Complications	No Stoma		Cecostomy	
	No.	%	No.	%
Probably Related to Integrity of Suture Line				
Severe peritonitis	4	2.5	0	...
Mild peritonitis	1	0.6	0	...
Abscess (intra-abdominal or pelvic)	2	1.3	1	1.5
Fecal fistula	2	1.3	2	3.0
Probably Unrelated to Integrity of Suture Line				
Stenosis (suture line)	3	1.9	0	...
Small bowel obstruction	0	...	4	6.0
Persistent cecostomy	0	...	5	7.5
Wound dehiscence	3	1.9	1	1.5
Unexplained fever	5	3.0	1	1.5
Wound infection	6	3.8	3	4.5
Thrombophlebitis	1	0.6	0	...
Pyelonephritis	1	0.6	0	...
Coronary occlusion	0	...	1	1.5
Pulmonary infarct	0	...	1	1.5
Cardiac arrest	1	0.6	0	...
Irreversible shock	0	...	1	1.5

CASE REPORTS

Some of the cases in each group in which complications arose have been abstracted for more detailed consideration. Only those cases are discussed in which fecal leakage from the site of anastomosis or from the cecostomy may have been a factor in producing the complications.

Group I—No Proximal Stoma

CASE I. (No. U-4069.) A fifty-five year old woman underwent resection of the colon with closed end-to-end anastomosis after preparation with sulfasuxidine.® The pathologic diagnosis was adenocarcinoma of the rectosigmoid colon. Continuous gastric suction was instituted postoperatively but the patient died suddenly on the seventh day following operation. Autopsy revealed generalized peritonitis and free fecal material within the abdomen.

The exact site of the perforation could not be determined because of the extensive inflammatory reaction but the presence of fecal matter in the abdomen would indicate leakage from the colon. This sequence of events and the autopsy findings suggest that a rather sudden and profuse discharge of bowel contents occurred into the peritoneal cavity, resulting in collapse and death.

CASE II. (No. U-137397.) A sigmoid colectomy was performed in a sixty-nine year old woman after preparation with sulfasuxidine. A portion of the colon that was diseased with diverticulitis was removed, and a previous sigmoid colostomy was resected. Owing to the disproportion in size of the segments of colon resulting from the colostomy, an open side-to-side anastomosis was performed. On the fourth postoperative day signs of peritonitis developed and free air was observed by roentgenogram in the peritoneal cavity. The patient died two days later despite intensive therapy. Permission for autopsy could not be obtained.

Because of the pneumoperitoneum, leakage from the large bowel was thought to be the most likely cause of death. Mesenteric thrombosis with secondary perforation was also considered. A perforated gastric or duodenal ulcer was a remote possibility. An unusual feature of this case, and one which is difficult to evaluate, was the difference in size of the two segments of colon.

CASE III. (No. U-165242.) This patient was a thirty-one year old woman in whom inflammatory necrosis of the colon developed which required resection of the sigmoid colon

following radiation therapy for carcinoma of the cervix. A closed end-to-end anastomosis was performed. Since this lesion was not anticipated, there was no preliminary preparation of the bowel. Gastric suction was utilized postoperatively. The patient convalesced satisfactorily until the eighteenth postoperative day when a tender mass was discovered in the left lower abdomen. On surgical exploration matted loops of small bowel and exudate were found in the region of the previous colon anastomosis. Drainage was performed and the patient subsequently recovered with antibiotic therapy.

The inflammatory reaction might have resulted from the original disease process, but fecal contamination from the suture line would seem to be the more likely cause of this condition.

Case IV. (No. U-125953.) An eighty year old man underwent resection for carcinoma of the rectum, following which an open end-to-end anastomosis was performed. A rectal tube was passed above the anastomosis for decompression and the perirectal space was drained through the buttock. On the tenth postoperative day a fecal fistula developed through the drainage site; it was still present at the time of dismissal from the hospital approximately one month later.

The advisability of using a rectal tube in such instances is controversial, but in this particular case the influence of the tube is obscure. Some surgeons believe that it is preferable not to employ a tube that must pass across a suture line. Because of the level of anastomosis, technical difficulty and impairment of blood supply to the sutured areas may have been responsible for the fecal leakage in this case. Another factor is the use of perirectal drains, which are thought by some to contribute to the development of fecal fistulas.

Case V. (No. U-162049.) A six year old boy was treated with a Swenson-type resection of the rectosigmoid colon for Hirschsprung's disease. Generalized peritonitis developed during the first week after operation and was followed by subphrenic abscess, small bowel obstruction and multiple intestinal fistulas. These complications resulted in death in about two months. At autopsy a breakdown at the site of anastomosis was found to be the primary source of contamination.

Hirschsprung's disease presents a special problem because the dilated and hypertrophied proximal colon may easily become overdistended. Frequently, several weeks or months are required for the bowel to return to normal after a Swenson operation. Cecostomies are difficult to manage in children and are not recommended by Swenson, but perhaps such a procedure should be considered under these circumstances.

Case VI. (No. U-120952.) A forty year old woman underwent resection of the colon with closed end-to-end anastomosis of the colonic segments for carcinoma of the rectosigmoid colon. Abdominal pain, fever and signs of peritonitis occurred on the fifth postoperative day. These symptoms subsided in several days with penicillin and sulfadiazine therapy, and there were no further sequelae.

Peritonitis was probably not secondary to a significant breakdown at the suture line in this case, since antibiotics could not be expected to aid sufficiently in localization to prevent fecal fistula or abscess had fecal leakage occurred.

Case VII. (No. U-29201.) A double stoma sigmoid colostomy was excised in a fifty-three year old woman and open end-to-end suture of the bowel segments was performed. Gastric decompression by means of a Levin tube was used. A fecal fistula developed in the abdominal wound on the tenth day after operation; this closed spontaneously two months later.

Undoubtedly the fecal fistula resulted from a breakdown at the site of anastomosis, but because of limiting factors generalized peritonitis did not occur.

Case VIII. (No. U-200626.) A sixty-seven year old man underwent sigmoid colectomy for a large inflammatory mass secondary to diverticulitis. An open end-to-end closure of the colon defect was performed and continuous suction was instituted. No significant complications developed until the fourth postoperative day when severe abdominal pain, fever, tachycardia, shock and death occurred within a twenty-four-hour period.

The presence of a chronic inflammatory process in the tissues of the operative area was an unfavorable factor in this case and may have contributed to the suture line leakage. Because of this condition a preliminary fecal diversion by transverse colostomy or complementary cecostomy might have been indicated.

Case IX. (No. U-128091.) An inflammatory lesion secondary to diverticulitis of the sigmoid colon was resected in a fifty-nine year

old man. A closed end-to-end anastomosis was performed. On the tenth postoperative day fever and diarrhea developed. These symptoms continued intermittently, and examination six weeks after operation revealed tenderness in the lower abdomen and a tender mass rectally in the posterior midline. The inflammatory process subsided under antibiotic therapy about two months postoperatively.

These symptoms and findings are consistent with those of pelvic abscess, which probably was secondary to fecal leakage from the suture line. Reactivation of the previous inflammatory process in adjacent pelvic structures is also to be considered.

Group II—Complementary Cecostomy

CASE X. (No. U-165035.) A fifty-three year old man underwent resection after preparation with sulfasuxidine, and open end-to-end anastomosis for carcinoma of the rectosigmoid colon was performed. A tube cecostomy was established at the same procedure. Penicillin, streptomycin and sulfasuxidine were given after operation. On the eleventh day the postoperative course was complicated by a fecal fistula which presented through the abdominal wound. The fistula closed spontaneously about two months later.

In this case cecostomy did not prevent leakage of fecal material from the bowel, which illustrates the fact that a cecal stoma does not completely divert the fecal stream.

CASE XI. (No. U-191134.) A fifty-seven year old woman was treated with resection of the left colon and open end-to-end anastomosis of the rectosigmoid colon. The lesion was adenocarcinoma but the patient had received radium and x-ray therapy nine months previously for squamous cell carcinoma of the cervix. A complementary tube cecostomy was established. During the postoperative period the patient experienced fever and a "bearing down" pain in the pelvis. On the eighteenth day a fecal fistula going into the vagina was apparent. Examination revealed an opening in the left fornix which communicated with an abscess cavity. It was assumed that leakage had occurred at the line of suture, resulting in an abscess which ruptured into the vagina. A transverse colostomy was performed to divert the bowel contents but purulent discharge from this area continued.

Radiation therapy undoubtedly rendered the tissue less favorable for anatomosis in this case. In spite of the cecostomy which was performed as a precautionary measure, a breakdown at the suture line occurred and resulted in abscess formation. An additional compromising factor was the unprepared condition of the bowel at the time of operation.

CASE XII. (No. U-207200.) A seventy-three year old man underwent sigmoid colectomy for diverticulitis and polyps. An end-to-end closed type of anastomosis was performed and a tube cecostomy was established at the same procedure. On the thirteenth postoperative day a wound dehiscence developed which required closure with through and through sutures. At that time an abscess was found in the anterior abdominal wall between the left rectus wound and the cecostomy. The patient was given intensive antibiotic therapy. The cecostomy required operative closure but the cecal fistula recurred and a second closure was necessary. The patient eventually recovered and was discharged on the sixty-ninth postoperative day.

The abdominal wall abscess and wound dehiscence are best explained by leakage from the cecostomy. In this case hospitalization and morbidity were prolonged as a result of the complementary cecostomy.

COMMENTS

As noted from these cases, complications resulting from fecal leakage were more common and more severe when a complementary cecostomy was not performed than when the proximal decompressive vent was established. Attention is particularly directed to the four cases of peritonitis resulting in death when no cecostomy was performed. In these fatal cases the onset of postoperative symptoms was usually acute, indicating sudden decompression of the colon through the site of perforation. By similar reasoning, a high intraluminal pressure was probably present within the bowel prior to rupture through the suture line.

On the other hand, there were no instances of generalized peritonitis and no deaths attributable to fecal contamination among the cases in which a complementary cecostomy was established. This comparison is more significant when one considers that cecostomies were usually performed when conditions for anastomosis were unfavorable. It should be remembered that cecostomy does not divert the fecal stream; the purpose of this complementary

procedure is to provide an outlet for excessive accumulation of gas or stool within the colon. From an analysis of the complications it can be concluded that overdistention of the large bowel was prevented in this group of patients.

Cecostomy cannot be considered a substitute for transverse colostomy, in which the fecal stream is completely diverted from the distal bowel. Transverse colostomy has a definite place in operations on the colon, but this study has been concerned only with examination of the role of cecostomy. Therefore no evaluation of transverse colostomy or comparison with cecostomy has been attempted herein.

The tube cecostomy is not difficult to perform but is of some inconvenience. Complications arising from the procedure itself were few; these included one abdominal wall abscess, one incisional hernia and five fistulas which required closure.

From this study it is apparent that complementary cecostomy is a useful procedure and should not be excluded from the armamentarium of the surgeon. It would seem to be primarily indicated in cases in which conditions are not ideal for colon anastomosis. Such factors as partial impairment of venous or arterial blood supply, subserosal hemorrhage, edema and fibrosis are important in this regard. A significant disproportion in size of the anastomosed segments, technically difficult closures low in the pelvis, unprepared bowel and the large atonic bowel of Hirschsprung's disease are also compromising situations. Under these circumstances the extra safety precaution of a proximal cecal vent can be expected to prevent overdistention of the large bowel.

SUMMARY

1. The complications arising from 226 cases of resection of the colon for various types of lesions have been reviewed. Only non-obstructive cases of primary anastomosis distal to the ascending colon are considered.

2. The incidence and severity of complications attributable to leakage from the suture line or perforation of the large bowel were lower in the group of sixty-seven patients treated with complementary cecostomy. In contrast to the group in which no proximal stoma was established, conditions of anastomosis were such in most of the cases in which complementary cecostomy was performed that complications were to be expected. The difference between the two groups, therefore, appears to be significant.

3. Complementary cecostomy is still a useful procedure and should be considered when ideal conditions for bowel anastomosis are not present.

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Congenital Aganglionic Megacolon

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As recently as 1947 it could justifiably be said "the surgical treatment of megacolon, although, perhaps, statistically more satisfactory than the use of medicaments, is far from ideal and such methods of operation as entero-anastomosis, drainage procedures, resection of segments of the bowel, and so forth, although they yield satisfactory results in many instances, have utterly failed to give relief in many other cases."[2] At that time it could also be said that "congenital megacolon colitis is a poorly understood disease for which no really satisfactory method of treatment has yet been devised."[15]

As is customary in those instances in which the etiology of a disease is one of speculation rather than knowledge, numerous theories were proposed in the search to determine what was the actual pathology in Hirschsprung's disease. Investigators were well aware that the etiology remained hidden. It is a matter of not infrequent note that once a discovery is made, it appears to have been so simple and apparent that it is a wonder it was not made long before. That is the situation in regard to the condition known as Hirschsprung's disease or, now more accurately termed, congenital aganglionic megacolon. With its specific etiology now clear, the wonder is, indeed, that it was not discovered long ago.

Many anatomists and physiologists had indicated the location of the abnormality. As early as 1901 in a report of one case of megacolon, Tittel[22] observed that the ganglion cells of the myenteric plexus of the large bowel showed signs of degeneration and were scanty as well at different levels. In a paper on megacolon in 1907, Hawkins[9] postulated the idea of a physiologic obstruction due to a neuromuscular defect as the cause of the disease. In 1920 and in 1924 Dalla Valle[6,7] reported two cases of congenital megacolon occurring in two brothers. In each instance he demonstrated the absence of nerve cells in Auerbach's plexus in the distal, undilated portion of the bowel. Cameron[4,5] reported inflammatory cell replacement of the ganglia of the myenteric plexus in the distal, undilated portion of the bowel in 1927 and 1928. Etzel[8] described absence of the nerve cells of the normal-appearing distal, large intestine in four cases of megacolon. In 1935 Perrot and Danon[18] reported a case of an autopsied fifteen-day old infant whose death from intestinal obstruction was attributed to a physiologic obstruction resulting from poor development of the myenteric plexus. In 1938 Robertson and Kernohan[19] reported the results of study of a boy whose death resulted from a typical case of megacolon. They reported that the ganglion cells and fibers of the plexus of Auerbach were definitely smaller than normal, vacuolated and the ganglion cells were absent or very imperfectly formed. They noted these same findings in several other cases of megacolon. In 1948 Whitehouse and Kernohan[24] reported a very excellent study of eleven cases of congenital megacolon. They conclusively demonstrated the absence of the ganglion cells of the plexus of Auerbach in the distal, undilated portion of the bowel and showed that this absence was not due to inflammatory change, vacuolation or any other replacement of ganglion cells, but rather was due to a complete absence of the cells which had never been present. This was emphatic support for the congenital basis of this disability. They further added support to this concept in their study of five cases of secondary megacolon. In no instance in these latter five cases was there absence of the ganglion cells of Auerbach's plexus.

In 1923 Ishikawa[12,13] stated that interruption of the sacral parasympathetic fibers to the colon was the cause of megacolon. Adamson and Aird[1] sectioned the same fibers in their work on cats and produced megacolon. Kleinschmidt[14] was able to verify this. From these factors it is apparent that much evidence existed to indicate that there was some neurogenic factor which was the cause of this disease. On this basis there evolved the idea of lumbar

sympathectomy as a specific procedure for this disease. While beneficial results were claimed to derive from this procedure, many failures were reported as well. The disease was still uncomprehended. With the mistaken idea of the dilated portion of the bowel as the seat of pathology, resections of this segment of the bowel were undertaken. Again the results of this were equivocal. Spasm of the sphincter ani was also presumed as a possible cause of the disability and attempts were made to rectify the pathology by eliminating this factor. All these measures simply skirted the actual facts. There was a factor of neurogenic imbalance but the absence of the ganglion cells of the myenteric plexus was the precise cause of it. There was a factor of obstruction, not due to an organic cause, but the result of a physiologic obstruction. There was the factor of inspissated feces resulting from marked dehydration due to the increased length of intestine with greater water-absorbing surface which, in turn, was secondary to the physiologic obstruction. All these factors fringed on the precise cause of this condition but none was quite accurate.

In 1948 Swenson and Bill[20] reported on a study, made in the previous two years, of twenty patients in whom a clinical diagnosis of congenital megacolon had been made. By means of a special technic they were able to demonstrate an area of spasm in the rectosigmoid or rectum. In the milder cases among these twenty the treatment suggested by Law[16] had been successful. Colostomies performed proximal to the area of spasm in six patients had relieved them completely. In three of these recurrence of the disability ensued when closure of the colostomy was performed. They, therefore, believed that removal of the area of spasm in its entirety would relieve the functional obstruction. To do this they devised an entirely new modification of the procedures described by Maunsell[17] and Weir.[23] The procedure was performed on dogs and gave such encouraging results that the operation was performed on three patients with excellent results. By August, 1950, Swenson[21] was able to report on fifty-two cases with excellent results in fifty-one and an anticipated similar result in the fifty-second. (Too distal a resection had been performed, requiring a second operation with a more proximal resection.) Stephens et al.,[3] who had observed Swenson's work, were able to report consistently successful results as well.

In March, 1951, Hiatt,[10] who had been working along lines similar to Swenson, published a paper on the pathologic physiology of congenital megacolon, and clearly expounded the disturbance which was present. He followed this at the same time with a paper[11] describing his modification of the procedure described by Swenson and Bill, and reported its use in twenty-three patients.

PATHOLOGIC PHYSIOLOGY

Only a proper understanding of the anatomy and physiology will make clear the pathologic disorders present in this disease. The nerve supply of the large intestine consists of two plexuses: (1) Auerbach's or the myenteric plexus which lies between the two muscular coats and, (2) Meissner's plexus which lies in the submucous layer. A peristaltic wave in the colon is a muscular contraction passing from the proximal to the distal part in a continuous manner. This is mediated through the Auerbach plexus with the ganglia serving as control stations for the nervous impulse so that the latter is graded and orderly, reaching the musculature at only one point at a time and causing that point to contract; and then passing in a sequential, regulated manner to the next distal point, causing the latter to contract while the previously contracted point relaxes. In this manner a well regulated peristaltic wave passes along the entire colon, from the cecum to the rectum. The time occupied in the passage of this wave from the beginning to the terminus of the large intestine is easily measurable by the eye. However, for all practical purposes the passage of an impulse along a nerve fiber may be considered instantaneous. If the nerve impulse were carried along a segment of the colon at this speed, it is readily apparent that such a segment would contract throughout its length simultaneously; there would be no graded impulse and there would simply exist a spastic contracture along such a segment of bowel which, with the passage of the impulse, would relax along its entire length simultaneously. It is apparent that no impetus exists to propel anything along the lumen of such segment forward or, for that matter, backward. Anything within such segment of bowel will simply be squeezed out at either end, orad and caudad. The designation of this disease as congenital

aganglionic megacolon describes the disease precisely. It is congenital and aganglionic because of the congenital absence of the ganglia of the myenteric plexus in the part of the bowel distal to the dilated portion. The disease is, in fact, in the distal *undilated* portion of the large intestine rather than in the *dilated* portion which contributes the word megacolon to the designation of the disease. The dilated portion of the bowel is, indeed, entirely normal; its greatly increased lumen, thickened wall and elongation are entirely physiologic reactions of normal bowel to a chronic obstruction *distal* to it. In the narrowed segment distal to the dilated portion of the colon, the ganglia of Auerbach's plexus are absent but nerve fibers are present. (The nerve fibers are non-myelinated and lie where Auerbach's plexus would normally be situated. These non-myelinated nerve fibers are not present to any marked degree where the myenteric plexus is present. The significance of these different fibers is unknown.[23]) The length of this segment is dependent directly upon the length over which the ganglia are missing. When the nerve impulse from the proximal, normal portion reaches this part of the bowel, an intense spastic contraction takes place, the lumen of the bowel is greatly contracted, if not entirely eliminated, the normal peristaltic wave reaching it is ended and with it the forward propulsion of the bolus from the proximal, normal portion. In effect, an almost complete obstruction is present at this junction of the normal with the aganglionic segment of the bowel. A vicious cycle is now set up. As the feces from the normal bowel reaches the aganglionic portion, the momentum imparted to them by the peristalsis propels some of them into the latter segment. As the forward movement behind continues, feces are packed into the first portion of the narrowed part of the bowel. This part of the fecal stream can move forward only by sufficient push from the propulsive efforts of the bowel orad to it. Meanwhile, though the aganglionic part of the bowel is incapable of peristaltic function, its other functions are not impaired. Water absorption from the feces in it continues and as it does the feces become drier and harder. The pounding from behind continues. An impaction now results, providing a stronger block to the feces constantly being propelled into the aganglionic portion. With the feces now backing up into the normal bowel, dilatation of the latter occurs. If the blockage is complete, *acute* intestinal obstruction results, in no manner different in result to the proximal part of the bowel than if an acute volvulus were to occur in the narrowed segment. It is characteristic of these patients that they do have episodes of acute intestinal obstruction. This results in the death of many of these infants at an early age. If the obstruction is not relieved all the sequelae of acute intestinal obstruction ensue up to death. Swenson and Bill noted that when proximal colostomy was performed as a lifesaving measure in six of their cases, the symptoms of the disease completely disappeared. When the colostomies were closed in three of these, prompt recurrence of the disease took place and full relief was again provided only by re-establishment of the colostomies. However, where complete obstruction does not occur, a chronic obstruction results and it is in this aspect of the disease that the characteristic picture of congenital aganglionic megacolon appears. With the piling up of the feces in the proximal, normal portion, the latter becomes secondarily dilated. As this fecal accumulation increases, the dilatation increases. As the dilatation continues the peristaltic waves become more forceful. As is true of any muscle in the body, increased use results in hypertrophy. The hypertrophy taking place here refers to both the circular and longitudinal muscle. With the hypertrophy there is, of course, thickening of the wall of the bowel as well as lengthening. In no other physiologic manner can the dilated, lengthened and hypertrophic bowel wall be explained. This dilatation and lengthening of the bowel provide a tremendously increased mucosal surface. As a result of this, continued over a period of time, the proximal, *normal* bowel becomes tremendously dilated with dehydrated feces, distending the abdominal wall until the characteristic picture of the child with the tremendously dilated abdomen, the flaring ribs, the spindly legs and the retarded development appears.

CLINICAL COURSE

With the proper use of enemas and other non-operative means of care, these children are not as severely disabled, but their disability is nevertheless marked. Hiatt has pointed out the danger of the enema itself when it is of the tap-water variety. He has shown that the danger of the tap-water lavage

consists in the very rapid absorption of the hypotonic solution through the greatly increased absorbing surface combined with the increased hydrostatic pressure. The result is water intoxication and these patients, not uncommonly, are found to be in extreme weakness and pallor with marked sweating following this type of enema. He ascribed the death of one of these patients, occurring immediately after such enema, to this fact. This is another factor accounting for the small number of these patients reaching adulthood. To minimize the dangers of the enema in these patients he has recommended a solution of 7 per cent gelatin which has an osmotic force equal to that of the circulation.

As is not unusual when one congenital defect exists, others often accompany it. Swenson investigated twenty patients with aganglionic megacolon by means of cystograms. He found that nineteen of them showed hypotonicity of the bladder, the bladder capacity of these patients being far above average before any detrusor contractions occurred. This is an indication of a deficient pelvic parasympathetic nerve supply. This is a matter of importance, for in the course of freeing the rectum prior to its removal from the pelvis, as is done in the surgical treatment of this condition, injury to the parasympathetic nerve supply to the bladder may easily occur since their precise course is unknown and the nerve fibers are too small to be dissected out.

DIAGNOSIS

The diagnosis of congenital aganglionic megacolon is not too difficult. At or shortly after birth obstinate constipation becomes apparent. By means of enemas alone these children are able to evacuate their bowels. So long as enemas are diligently given, these children will have bowel movements. Despite the administration of enemas the overwhelming majority of children will appear with a greatly distended abdomen, although not necessarily sick. Their parents will report that they eat well if they are given enemas with any degree of regularity. Some will definitely show physical and mental retardation; others will not. There will usually be a history of treatment by medical means over a long period of time, but this treatment will not have affected them any more than when they received enemas alone.

Some of these patients may be seen as newborns in an acutely obstructed condition. There the need for differentiation will be only between congenital aganglionic megacolon and organic obstruction, complete or incomplete. With aganglionic megacolon a history will usually be obtained of some anal expulsion of feces following birth. In those newborns with complete organic obstruction there will never have been a bowel movement and the scout film of the abdomen will show the point of obstruction inasmuch as there will be no bowel gas noted distal to that site.

In those infants and children older than the newborn, acute intestinal obstruction may also occur. These patients will have a history pathognomonic of this disease. Certainly no legal statute exists stating that these children cannot develop an obstruction due to other causes. The differential diagnosis here should not cause serious difficulty.

TECHNIC

Where the obstruction is complete, exploratory laparotomy will be required with the performance of the shortest possible procedure consistent with saving the patient's life. This will usually consist of a transverse loop colostomy definitely proximal to the contracted segment. It would usually be unwise to attempt to give an enema with the idea of loosening the impacted feces and thereby allow the gas behind to be expelled. The increased intracolonic pressure may possibly be enough to result in a blowout of the tightly distended colon. It should be a matter of note that in any *acute* obstruction there is insufficient time for the bowel musculature to become hypertrophic. Consequently the bowel wall proximal to the obstruction is thinned. Bowel wall hypertrophy occurs only where there is adequate time for development as in *chronic* obstruction.

When no emergency exists, the patient may be fully assayed and prepared for definitive surgery. While no dogmatic rules about performance of this operation relative to the size of the patient can be made, the child with this disease who is two years of age or older is a suitable candidate. In those younger, a transverse colostomy well proximal to the narrowed, distal segment should be performed until the child's size is sufficient to permit performance of the specific procedure. Those who are experienced in performing this procedure can

certainly execute it in smaller children. On the average, however, it is desirable to wait until the patient's size is such that the structures may be seen and dissected with greater accuracy.

The operation consists of removal of the entire narrowed, distal segment, the transitional area and a variable part of the distal, dilated part of the colon. Beside the customary means used to prepare a patient in this age group for major abdominal surgery of an elective nature, it is desirable to decompress the dilated bowel before going to surgery. By means of diet, enemas and intestinal antiseptics this can be obtained, as well as providing a sterile, colonic lumen. It is also highly desirable to intubate a vein, usually the greater saphenous at the ankle, with a polyethylene catheter prior to the start of surgery. Once the patient is properly prepared the procedure used is the operation devised by Swenson with Hiatt's modification.

Entrance to the peritoneal cavity is provided by either a lower left, vertical rectus incision or an oblique one starting in the region of the right pubic spine and extending in an oblique line across the midline, cutting the left rectus muscle and extending to the left flank. The finding of the junction of the dilated, hypertrophied segment with the distal, narrowed segment (the transitional area) is the point at which bearings are taken. The superior hemorrhoidal vessels are found and clamped along the transitional segment. The transitional portion and all the large bowel distal to it are now dissected free from all the structures attached to them. It must be constantly kept in mind that in this dissection it is the absence of the ganglion cells lying between the longitudinal and circular musculatures that is the cause of this disease. Therefore, the removal of the tube of bowel where this deficiency exists without the inclusion of any attached structures is the desired dissection. Furthermore, since so many of these patients have poor innervation of the pelvic viscera, disturbance of any of the structures other than the bowel itself is highly undesirable. The narrowed segment is, therefore, stripped down very closely along its outer coat to the insertion of the levator ani into the anus. Because the normal but dilated and hypertrophied portion has been propelling feces into the proximal part of the abnormal segment, some dilatation of a variable length of the proximal part of the latter is present. For this reason it is necessary to resect a variable portion of the dilated segment orad to the transitional area. More precisely, frozen sections of the muscularis taken at intervals along this part of the bowel will reveal where the ganglia are present in normal number. This may, however, result in undue prolongation of an already lengthy procedure. By pathologic examination 12 cm.[21] and 20 cm.[10] have been suggested as a sufficiently safe orad point of resection. In line with those suggestions the length of bowel resected will vary with the distance between the transitional area and the anus. It may require anastomosing the splenic flexure or even the transverse colon to the anus. The blood supply to the unresected portion of the bowel must, of course, remain unimpaired. It may be found that the only thing preventing approximation of the point of resection of the bowel wall to the anus without tension is the inability of the blood vessels to stretch that distance. Where this is so, the mesentery must be cut close to its origin and the blood vessels hindering this movement must be ligated close to their origin, usually the inferior mesenteric vessels. With that done the arcades and the marginal artery are preserved, permitting the vascular supply to remain intact and at the same time allowing the necessary mobility. This having been accomplished, attention is now directed to the perineum. The anus is dilated, an Allis clamp inserted from outside the body into the rectum and directed by a hand in the abdomen to as high a position as possible, the bowel is clamped and is drawn down to the anus and out, intussuscepting the bowel through the anus. It is drawn out far enough so that the point which has been elected for anastomosis to the anus is brought into proper position for the performance of the anastomosis on the perineum. A two-layer anastomosis may be done here, cutting away at the same time the diseased bowel. At the completion of this step the newly formed anastomosis is pushed back into the body through the anus. A drain may or may not be inserted into the presacral-retro-anastomotic area through a stab incision between the tip of the coccyx and the posterior margin of the anal ring.

CASE REPORTS

CASE 1. D. L., a six year old boy, was seen with the complaints of abdominal distention,

frequent episodes of illness and obstipation. Since the second month of his birth the parents could barely recall when he had had a bowel movement spontaneously. Enemas and cathartics were used regularly to obtain bowel movements. There had been episodes when he was particularly ill and when he would finally have a bowel movement after several attempts. At such times the excreta consisted of very firm, scybalous balls. Between such episodes the feces were very firm as well. The child went to school and was an average student. His mixture with his classmates was greatly limited because of his inability to keep up with their activity. He had been under the care of doctors who had treated him medically with very little improvement above that obtained by enemas and cathartics alone.

Physical examination revealed a pale, white boy who appeared his age of six but who definitely lacked the vigor seen in a well child of that age. His abdomen was the most prominent part of his anatomy because of its marked distention. It was symmetrically distended and bulged the ribs outward, causing them to flare. Several large veins coursed over the abdomen. On palpation the abdomen was firm but not hard. No tenderness was present unless heavy and deep palpation were done. No masses could be felt. There was no rebound tenderness. The extremities were somewhat thinner in appearance than a normal child of the same age. He was pale and the skin, as a result of this and the absence of blemishes, had an "ethereal" appearance to it. The only other abnormality of note was a limp in the left lower extremity due to Perthes disease of the left hip.

Barium enema revealed the typical findings in this disease. The radiologist's report follows: "Examination of the colon, by barium enema, demonstrates that the rectum and distal sigmoid did not distend to the degree that is ordinarily seen in the course of a barium enema, but these structures were normal in contour. The proximal rectum extends directly superiorly in the midline to a point anterior to the interspace between L 4 and 5 and then turns anteriorly and to the right. At the point of turn the lumen fairly abruptly widens to about 3 times the caliber of the sigmoid distal to this point. The sigmoid is very long and this dilated portion extends to the right to overlie the lateral portion of the right ileum and then extends completely across the abdomen to the left side. No attempt was made to fill the proximal colon. Wide mucosal folds are visible in this dilated intestine."

The patient was prepared for surgery by means of daily enemas of physiologic saline until clear return, administration of oral sulfasuxidine and milk of magnesia and cascara cathartics. Orally the patient received daily multivitamin capsules and a low residue, high protein, high calorie diet. When the distention of the abdomen had been reduced to an almost normal appearance and the enema return showed soft stool without odor, the patient was subjected to the operation. His postoperative course was uneventful. He had a spontaneous bowel movement on the third postoperative day. Oral feedings were started that same day. Sutures were not removed until the tenth postoperative day and the patient was discharged on the thirteenth postoperative day. There has been no diarrhea and the patient has one to two formed, soft bowel movements daily. In the eighteen months since the operation the patient has shown a much more rapid rate of growth than previously and he has put on weight in accordance with it. The treatment of the Perthes disease of the left hip was started four months after the operation under orthopedic care and is continuing.

Case II. C. M., a two and a half year old girl, had had a few bowel movements immediately after birth but had also become distended abdominally within one month after birth. Treatment by the various medical procedures was carried out in conjunction with enemas; and when the medication was halted and the enemas alone used, the child did as well. Although enemas had been given daily there had always been present a marked degree of abdominal distention. No history of urinary difficulty was obtained.

Physical examination revealed a two and one-half year old girl who did not appear to be behind the developmental pattern for her age. She appeared to be fairly active. Her large protuberant abdomen, which in its state was symmetric, bulged up to the costal margins, causing the ribs to flare. Her hemic component appeared to be normal. The abdomen was firm but not hard, not tender and no masses could be felt. Neither liver nor spleen was palpable. No other abnormalities were noted. A barium enema revealed the findings

typical of the disease. The radiologist's report follows: "A preliminary film of the abdomen shows several markedly dilated gas-filled loops of intestine, undoubtedly colon, in the right abdomen and mid-line and several loops of small intestine, not dilated, and containing only a little gas, in the left abdomen. Examination of the colon by barium enema showed that the rectum and distal sigmoid were essentially normal in caliber, but beginning at about the mid-sigmoid, there was very marked dilatation of the proximal colon. The sigmoid extends upward and to the right so that the point of junction of non-dilated and dilated sigmoid is in the right upper quadrant. The post-evacuation film shows that the distal sigmoid and rectum has expelled most of the barium from that area, but the proximal sigmoid and the colon retained the barium. This examination shows evidence of megacolon. The narrow segment of intestine begins at about the mid-sigmoid and involves the distal sigmoid and rectum."

After four days of preparation (morning and evening saline enemas, milk of magnesia with cascara daily, and sulfasuxidine combined with a low residue, high protein, high calorie diet) the patient was taken to the operating room. The large bowel, extending orad from a point 2 cm. above the pectinate line (including the entire narrowed segment) and 20 cm. cephalad to the transitional area, was dissected free, intussuscepted through the anus and resected as the anocolonic anastomosis was performed on the perineum.

The postoperative course was uneventful. On the second postoperative day the patient started to have bowel movements of gelatinous consistency and was allowed up and about freely. By the fifth postoperative day she was eating a regular diet, her bowel movements were only two per day and she was discharged. Since that time (sixteen months ago) she has had no difficulty, her abdomen has receded to normal size and she has been normal in every respect for a child her age.

CONCLUSIONS

Experimental and pathologic observations over a long period of time, culminating in an operative procedure devised by Swenson to verify conclusions reached concerning the pathologic physiology of Hirschsprung's disease, have definitely established the cause of this disease entity and resulted in a curative procedure. An attempt has been made to clarify the steps in the development of the clinical entity long noted in this disease.

Two cases have been presented to illustrate the excellent results that can be achieved by operative correction of this congenital anomaly.

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KINSELL has had a very favorable experience using hormone therapy in addition to antibiotics in acute inflammatory surgical cases. Of course the hormones he used (ACTH or cortisone) are known to increase the breakdown of protein tissue and the loss of chlorides and potassium. Therefore, these patients need increased quantities of proteins intravenously and potassium chloride. These hormones also cause an increase in body retention of sodium, so the use of intravenous sodium should be greatly limited. Kinsell realizes there are certain contraindications to the use of these hormones, especially in patients with gastrointestional ulceration, insufficient renal function, congestive heart disease or tuberculosis. Many patients in a debilitated condition who need non-emergency surgery will make a better convalescence if treated by these hormones for two days prior to surgery and three days afterward. (*Richard A. Leonardo, M.D.*)

Gastrointestinal Adenosis Associated with Melanin Spots on Lips, Buccal Mucosa and Digits

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ANY segment of the gastrointestinal tract or any combination of segments may be the site of numerous adenomatous polyps. The literature is replete with case histories of hereditary adenosis of the colon and rectum. Therefore, only a few brief facts about this disease will be mentioned in this paper.

Hereditary adenosis of the colon and rectum has been well established as a clinicopathologic entity. The disease ends abruptly at the ileocecal junction. From a genetic standpoint it is mendelian dominent characterized by a single dominent gene. The transmission may be through either parent. About half of the children of an affected parent have the disease while all the children of those parents not affected are normal. (Fig. 1.)

In contrast, hereditary adenosis of the gastrointestinal tract associated with distinctive melanin spots on the lips, buccal mucosa and digits has not been recognized too frequently, and fewer than thirty proved cases have been reported in the literature. The syndrome has been adequately described by Jeghers et al.[1] Before his paper on the subject, published in 1949, the disease was not previously identified in the English literature and was recognized to a very limited extent elsewhere. Dr. Jeghers gave credit to Dr. Pentz of Holland for giving the first adequate description.

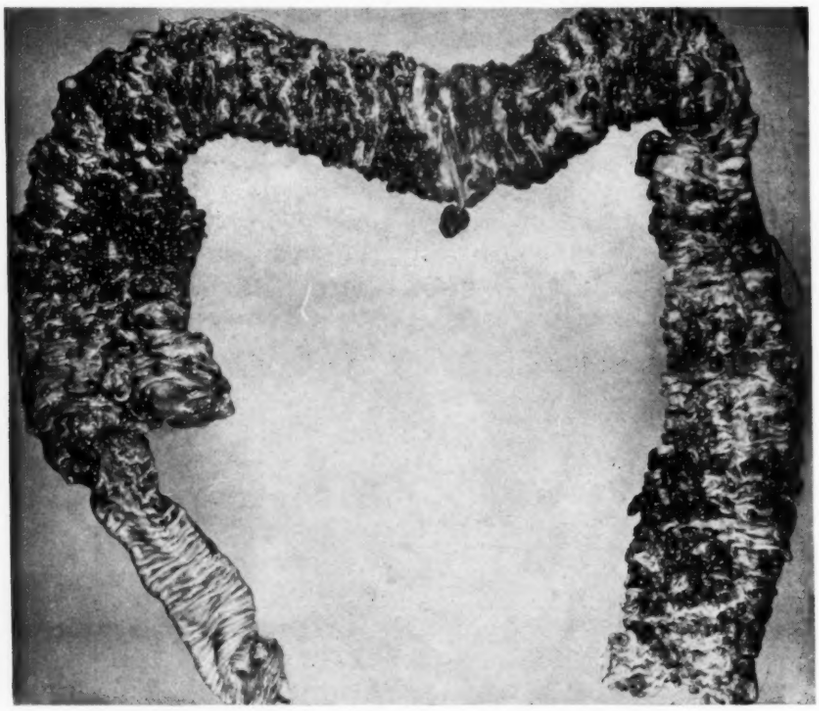

FIG. 1. Hereditary adenosis of the colon and rectum.

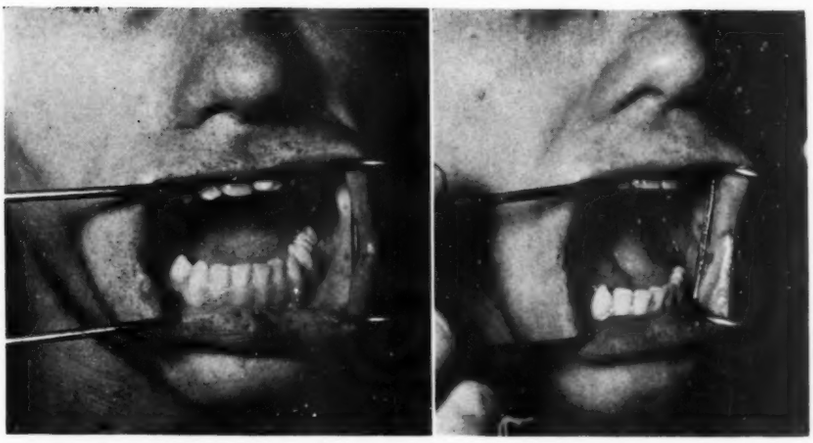

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FIG. 2. Case 1. Distinctive melanin spots on the lips.

FIG. 3. Same case. Distinctive melanin spots on buccal mucosa.

FIG. 4. Case 1. Melanin spots on digits.

CASE REPORTS

The following case is presented briefly to again draw attention to this interesting syndrome.

CASE 1. F. C., an eighteen year old white boy, was admitted to the Roswell Park Memorial Institute on October 9, 1951. His symptoms included generalized itching of the skin for one year, paraumbilical abdominal pain, fatigue associated with a weight loss of 15 pounds, and a discharge of blood from the rectum.

The patient's father and brother showed evidence of the disease; his mother and two sisters were uninvolved.

Physical examination disclosed distinctive pigmentation of the lips, buccal mucosa and digits. (Figs. 2 to 4.) The examination otherwise was not informative. Roentgenoscopy demonstrated numerous polyps in the colon, especially around the hepatic flexure. The stomach and small bowel were not examined. The sigmoidoscopic examination was negative. Surgery was advised and accepted.

On November 30, 1951, the abdomen was explored. A polyp measuring 2.5 cm. was located involving the jejunum 50 cm. from the ligament of Treitz. A partial obstruction was obvious as the jejunum above the polyp was dilated and hypertrophied. A polyp 80 cm. from the ligament of Treitz was discovered by palpation. Both polyps were removed. The stomach was free of any palpable pathologic disease. A one-stage colectomy with the establishment of an ileosigmoid colostomy was completed.

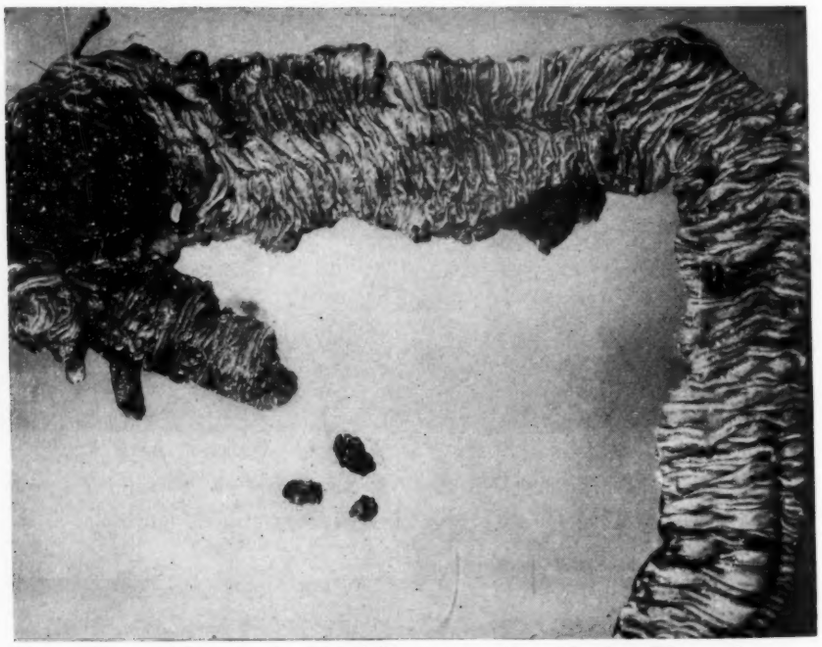

FIG. 5. Case 1. Adenosis of terminal ilium, appendix and colon. Three adenomatous polyps removed from the small bowel.

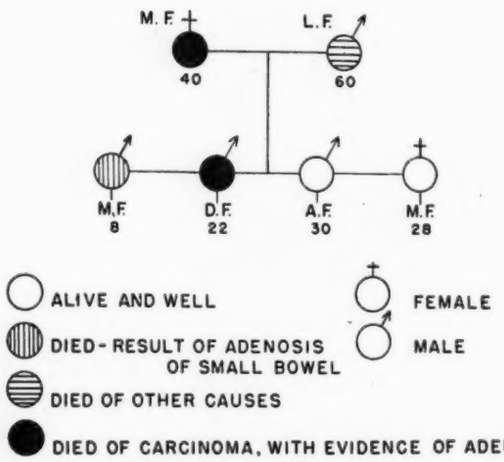

FIG. 6. Case II. Family history.

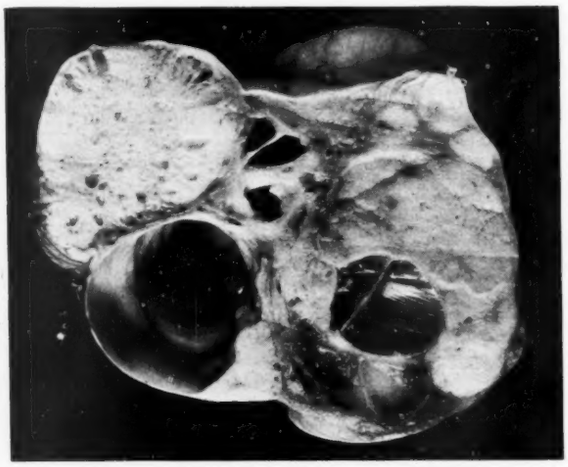

FIG. 7. Case II. Left ovary showing multiple cysts and malignant tumor.

From a gross inspection of the terminal ileum and appendix, which showed countless small polyps that escaped detection on palpation during celiotomy, one is impressed with the fact that the entire small bowel was similarly involved. (Fig. 5.)

The patient made an uneventful recovery and has been asymptomatic to date. How long before remaining polyps will increase in size and act as a nidus for an intussusception or cause an obstruction is an interesting speculation.

The role that inheritance plays as a factor in the etiology of adenosis of the gastrointestinal tract, other than the two clinicopathologic entities previously described, has not been established. The following case reports may add significant information about this subject:

CASE II. M. F., a forty year old woman, was admitted to the Roswell Park Memorial Institute on May 23, 1934. The family history is illustrated in Figure 6. The following symptoms were recorded: a lump in the right breast, vague lower abdominal discomfort and a sacroiliac backache.

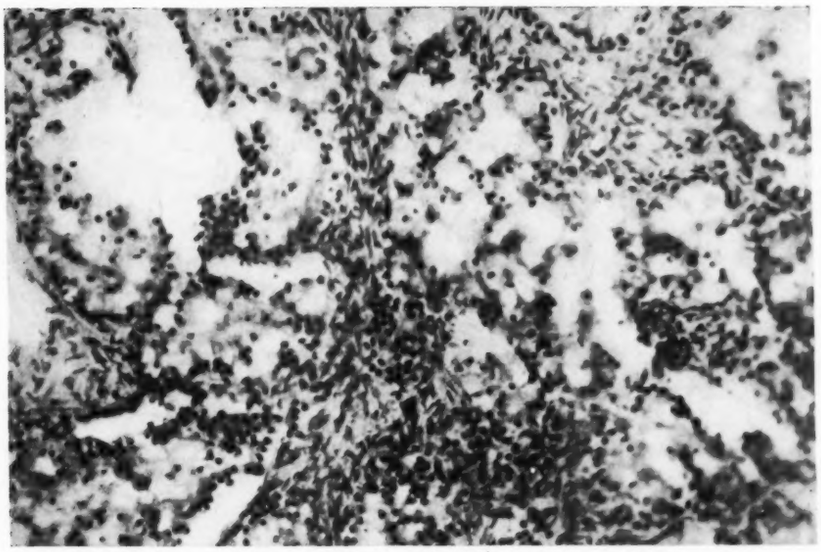

FIG. 8. Case II. Histopathology of malignant tumor of left ovary.

Physical examination disclosed evidence of a firm tumor mass, measuring about 6 cm. in diameter, involving the outer mid-quadrant of the right breast and fixed to the overlying skin. A biopsy specimen was removed; the histopathologic report was carcinoma.

Abdominal examination revealed evidence of a nodular mass in the pelvis adjacent to the pubis. On rectal and pelvic examination several nodular tumor masses were felt. A diagnosis of carcinoma of the left ovary with pelvic metastatic spread was considered.

Several days after admission the abdomen became distended and roentgenoscopy disclosed that a space-filling defect in the mid-descending colon was causing complete obstruction.

On sigmoidoscopic examination several small polyps were located in the upper rectum and lower sigmoid colon. One polyp was removed and reported as benign adenoma.

Cecostomy was performed to deviate the fecal stream. During this procedure a nodule from the omentum was removed and reported as metastatic carcinoma. The patient died on July 10, 1934.

Postmortem examination disclosed primary carcinoma of the left ovary with generalized abdominal carcinomatosis. (Figs. 7 and 8.) After histopathologic review of all malignant tissue it was concluded that the primary site of carcinoma was resident in the left ovary with metastatic involvement of the breast, descending colon, visceral and parietal peritoneum, and pleura. The gastrointestinal tract was either not examined or, if so, the findings were not recorded. Therefore, no information is available as to whether or not there was evidence of polyposis involving the gastrointestinal tract other than the upper rectum and lower sigmoid colon as disclosed on sigmoidoscopic examination.

CASE III. D. F., the twenty-two year old son of M. F. (Case II), was admitted to the Roswell Park Memorial Institute on December 8, 1948. The family history is given in Figure 6.

The following symptoms of two months' duration were recorded on admission: loss of appetite, frequent nausea and vomiting, progressive weakness, and weight loss of 20 pounds. Past history was irrelevant, except that for several years the patient had passed a small amount of blood mixed with the stool.

The salient finding on physical examination included emaciation, an enlarged nodular liver, an umbilical and periumbilical mass involving the abdominal wall and an upper perirectal mass typical of Blumer's shelf. Biopsy from the umbilical tumor was reported as metastatic adenocarcinoma. Gastrointestinal x-ray series reported a space-filling defect in the antrum of the stomach consistent with a primary malignant new growth.

Sigmoidoscopic examination revealed evidence of polyps in the upper rectum and lower sigmoid colon. Biopsy of a polyp was reported as benign adenoma. A postmortem examination was not conducted.

CASE IV. M. F., the eight year old son of M. F. (Case II), was admitted to the Mercy Hospital in Buffalo on January 4, 1942. The family history is given in Figure 6.

Symptoms on admission were: severe cramp-like pains throughout the abdomen, frequent

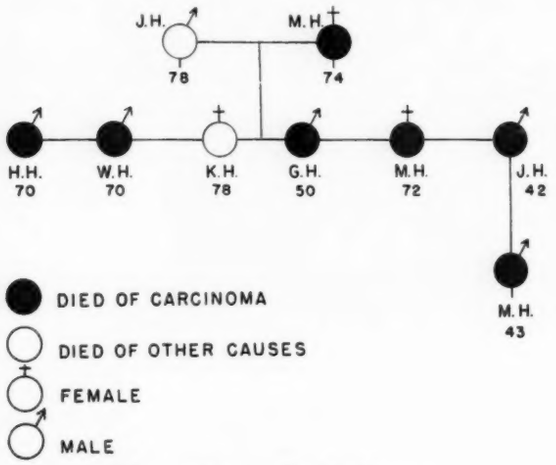

FIG. 9. Case v. Family history.

emesis and a discharge of large quantities of dark blood from the rectum. Physical examination revealed that the patient was in extreme shock; the abdomen was markedly distended.

The patient died a few hours after admission. Postmortem examination revealed the following findings: (1) A tremendous intussusception of the jejunum in the usual direction; (2) a polyp of the jejunum measuring 3½ by 3 by 2 cm. which acted as the nidus for the intussusception. Two smaller polyps were located in the small bowel; (3) the stomach contained several polyps; the largest, projecting from the lesser curvature, measured 2 by 1½ by 1½ cm. The large bowel and rectum were free of disease.

CASE V. M. H., a thirty-eight year old woman, was admitted to the Roswell Park Memorial Institute April 30, 1934.

The family history is shown in Figure 9. The patient's father, so it was stated in the family history, died from carcinoma of the rectum. Her grandmother died from carcinoma of the intestine. Four of five of her aunts and uncles died, it was stated by living members of the third generation, from carcinoma, the site unknown. Aside from the patient, other members of the third generation were not investigated.

The patient related a three-month history of alteration of bowel habits and a discharge of blood from the rectum. Complete physical examination was not remarkable except for annular ulcerating carcinoma of the upper section. Biopsy was reported as adenocarcinoma. Treatment consisted solely of high voltage x-ray therapy and the insertion of gold radon seeds into the tumor.

In 1934 a number of patients were so treated to evaluate this method of therapy. The radical abdominoperineal resection of the rectum, however, has been and still is our approach to the problem of carcinoma of the rectum.

The treatment in Case IV, however, was effective. The x-ray and radon seeds were lethal to the tumor, leaving a smooth stricture. The patient returned at intervals for dilatation of the stricture. She remained free of recurrence of carcinoma of the rectum for fifteen years. On March 21, 1949, she was admitted to another hospital with several days' history of severe abdominal pain. The hospital record revealed the patient to be in profound shock on admission. Her abdomen was markedly distended. A diagnosis of generalized peritonitis was made. The patient died one day after admission.

Autopsy findings were recorded as follows: (1) Diffuse fulminating peritonitis caused by a perforation of the pelvic colon a short distance above the rectal stricture; (2) annular constricting carcinoma of the transverse colon with solitary metastases to the liver; (3) diffuse polyposis of the stomach and the large bowel; the small bowel was free of pathologic disorder; (4) no recurrence of rectal carcinoma.

COMMENTS

Referring to Cases II, III and IV, it appears to us that the presence of benign adenomas in three members of the same family could not be explained on chance occurrence, but indicates that heredity played a role in the etiology.

It has been demonstrated that a number of patients suffering from hereditary adenosis of the colon and rectum have a proclivity for the development of tumors other than in the colon and rectum. Cases II, III and IV suggest that families harboring adenosis of the gastrointestinal tract may also have a cell instability favoring the change of somatic cells into benign or malignant tumors. Further study of similar case histories will be necessary to support this supposition.

In reference to Case v, I believe that diffuse adenosis of the stomach occurring synchronously with diffuse adenosis of the colon without involvement of the small bowel is a clinicopathologic entity and that heredity is a factor in the etiology.

We trust that these reported cases will stimulate a more energetic study of this problem.

CONCLUSIONS

1. A case of hereditary adenosis of the gastrointestinal tract associated with distinctive malanin spots of the lip, buccal mucosa and digits has been added to the number already reported.

2. To date sufficient evidence has not been recorded in the literature to show the role inheritance plays in the etiology of gastrointestinal adenosis when not associated with melanin spots on the lips, buccal mucosa and digits.

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Cook et al. believe, on the basis of a statistical study, that silent gallstones do not usually cause cancer of the gallbladder in more than 3 per cent of the cases and often the incidence is only 1 per cent. Hence, "prophylactive cholecystectomy" is unjustified because often the operative mortality is greater, not to mention other factors such as pain, expense and use of overcrowded surgical hospital facilities. (*Richard A. Leonardo, M.D.*)

Segmental Resection for Tuberculosis

ANALYSIS OF FIFTY CONSECUTIVE CASES

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ALTHOUGH the bronchovascular segment has been recognized for many years as the anatomic unit of the lung,[1–4] pulmonary resection by segments is of more recent popularity. The basic technic, described by Churchill and Belsey[5] and Clagett and Deterling,[6] in relation to the excision of the lingula in patients with bronchiectasis of the left lower lobe and the lingula has been extended progressively to other segments. However, the line of cleavage developed between segments is not so well delineated as are the fissures between lobes, and the pleural barrier to extension of infection is absent. Accordingly, the use of segmental resection on a large scale in tuberculous patients depends upon adequate preoperative control of the active, pneumonic component of the infective process so that the dangerous, latent focus of fibronodular, caseous or bronchial disease can be excised safely. Adequate chemotherapy is therefore indispensable. Since by definition segmental resection limits the excision to the portion of the lung actually involved, little functioning pulmonary tissue is removed. The diseased area has already decreased in size, and the rest of the lung has made its compensatory adjustments over a period of months, so that disproportion between the remaining lung and the pleural space is rarely severe enough to require specific management. The complications which accompany segmental excision are usually related to the artificial plane established at the time of operation, air leaks and incomplete expansions, and the mishaps encountered in any major surgery, rather than to space problems, pulmonary insufficiency and fulminating tuberculous infection. Since tuberculosis has a predilection for the apical and the posterior portions of the lobes of the lung, it is possible to remove (by segmental resection) significant lesions from the upper and lower lobes on one side. At a later date they may be removed from the other side without significant decrease in the pulmonary function of the patient, if pleural complications have been successfully avoided. Conversely, a patient with only one small residual, necrotic focus may have a more favorable prognosis by segmental excision of this lesion, provided the operation can be carried out without excessive danger.

To review our own results and to assess the complications encountered a study has been made of fifty consecutive segmental resections performed at the West Tennessee Tuberculosis Hospital, Memphis, beginning January 30, 1952, and ending October 19, 1953.

OBSERVATIONS

Indications. The clinical and radiologic indications for segmental resection are the same as for other resections in tuberculosis, with the added provision that the disease process be segmental in distribution and reasonably localized. Residual necrotic foci after long chemotherapy comprise the majority of lesions segmentally removed, but persistent cavities, solitary nodules and bronchial disease also are removed frequently. The indications for limiting resection to a segment rather than to more pulmonary tissue are: (1) The significant disease is localized to one or more segments; (2) segments of more than one lobe are involved; (3) maximum conservation of pulmonary function is obligatory either because of previous collapse therapy or resection, planned bilateral intervention, or reduced pulmonary function.

Preoperative Management. Most patients who are candidates for segmental resection for tuberculosis should have long courses of combined chemotherapy, and operation should be undertaken after serial films demonstrate stability of the lesion. An exception to this must be made in those solid foci suspected of

malignancy which must be operated upon early in order to make a diagnosis. The involved segments are identified as exactly as possible before operation by bronchograms and by the use of body section roentgenography in both postero-anterior and lateral planes. Usually bronchograms give more accurate information since the laminagraphic studies cannot take into account the shifting of the segments during healing and contraction. Bronchoscopy is performed prior to surgery to discover any endobronchial foci and to check anatomy. As in all surgery the final decision of the extent of the resection must be made at the operating table, with the chest open and after complete palpation of the lung. The information gained is combined with that available from preoperative studies and an appropriate operation is performed.

Technic. The surgical technic used in these cases has been developed by Churchill and Belsey,[5] Overholt et al.,[7–11] Clagett,[6] and Blades.[12] The following points are enforced strictly: (1) The segmental artery and the bronchus are isolated at the hilum of the lobe. (2) Nothing is clamped or divided until all structures are identified. (3) The segmental bronchus is clamped and divided in the operation as early as possible. (4) The separation of the segment is accomplished by traction and blunt dissection. Intersegmental veins are preserved. (5) No clamps are placed across lung tissue. (6) The segmental raw areas are not covered. Bronchiolar leaks may be sutured but alveolar leaks are not sutured. Absolute hemostasis is necessary. (7) The bronchial stump is closed simply with interrupted atraumatic® cotton, and an attempt is made to buttress the stump with adjacent tissue. (8) Tubes for drainage must be placed carefully to drain the segmental areas as well as the general pleural space. Usually two No. 26 French catheters with multiple holes are used. (9) Throughout operation the blood loss is calculated by the sponge weight method, and the blood is replaced as it is lost.[13]

Postoperative Management. Suction drainage is applied to the thoracotomy tubes with pressure maintained approximately at -15 cm. of water. Specific antituberculosis therapy is continued as in the preoperative period; nonspecific antibiotics are used for approximately one week. Early and complete expansion of the lung to fill the chest is necessary to prevent complications. Portable chest x-ray is taken four hours postoperatively and repeated at daily intervals. The drainage tubes are adjusted as needed. When drainage has stopped and the lung is expanded, the tubes are removed, usually in forty-eight to seventy-two hours. The standard measures are used to combat retained secretions and early ambulation is encouraged. Leaks in the lung and pneumothorax may occur as late as three or four weeks after operation and must be watched for and treated vigorously by tube drainage.

TABLE 1
SEGMENTS REMOVED AT RESECTION

Segment	No.	Total No.
Right lung		
Upper lobe:		26
Apical segment	9	
Apical subsegment	1	
Posterior segment	12	
Posterior subsegment	3	
Anterior segment	1	
Middle lobe:		1
Subsegment, lateral portion	1	
Lower lobe:		10
Superior segment	9	
Posterior basal segment	1	
Left lung		
Upper lobe:		29
Apical-posterior segment	14	
Posterior subsegment	4	
Anterior segment	4	
Anterior subsegment	5	
Lingula	2	
Lower lobe:		14
Superior segment	10	
Superior subsegment	1	
Lateral basal segment	3	
Total	80	80

Analysis of Material. Fifty consecutive operations were performed on forty-eight patients with two instances of bilateral segmental resection. Of the other forty-six patients, four had previous contralateral lobectomies. A single segment was removed in twenty-four operations, more than one in twenty-six cases. A total of eighty segments was removed. (Table 1.)

In five of the previously mentioned cases additional procedures such as decortication

and plication of the diaphragm were done at the time of resection. As pointed out by Chamberlain and Klopstock,[14] segments of the lung most frequently involved are the apical and the posterior segments of the upper lobe and the superior segment of the lower lobe.

TABLE II

Age of Patients (yr.)	White Males	White Females	Negro Males	Negro Females	Total Number of Cases
Under 10	0	0	0	1	1
10 to 20	4	6	3	1	14
21 to 30	5	3	4	2	14
31 to 40	0	9	0	0	9
41 to 50	4	3	0	0	7
51 to 60	2	0	0	0	2
61 to 70	1	0	0	0	1

TABLE III
COMPLICATIONS IN FORTY-EIGHT CASES OF PULMONARY TUBERCULOSIS

Complications	No. of Patients	Resections (%)
Spread (1):		2
Postoperative spread to ipsilateral lung	1	
Expansion difficulties (8):		16
Bronchopleural fistula	3	
Bronchopleural fistula with empyema	2	
Clotted hemothorax and bronchopleural fistula	1	
Localized fluid accumulation	1	
Asymptomatic delayed expansion	1	
Miscellaneous (5):		10
Transient radial nerve paralysis	2	
Hemorrhage from skin incision	1	
Pulmonary insufficiency	1	
Persistent positive sputum	1	

The patients ranged in age from five years to sixty-two years, ten of the forty-eight patients being over forty years. It is interesting to note that the ratio of white to non-white patients was approximately three to one. This fact seems to be related directly to the more advanced stage of the disease in non-white patients when first seen. (Table II.)

Results. There were no deaths in the fifty consecutive resections. In thirty-six patients (72 per cent) the postoperative course was smooth; while some type of major or minor complication developed in fourteen patients (28 per cent). An analysis of the complications is shown in Table III.

DISCUSSION OF COMPLICATIONS

Spread

CASE 22. J. T., a twenty-three year old Negro man, ran a persistently elevated temperature of 99°F. and above immediately after surgery. X-rays showed spread of the disease in the remaining lung tissue. The spread responded to chemotherapy and bedrest. The patient is now doing well.

Expansion Difficulties

CASE 42. L. T. S., a sixty-two year old white man, developed partial atelectasis two days postoperatively. This was aggravated by improper function of the tubes despite manipulation, and by the development of a bronchopleural fistula. This was treated for ten days by thoracotomy tube drainage and suction, with complete re-expansion of the lung and closure of the fistula.

CASE 1. N. O., a forty-nine year old white man, had the apical-posterior and the anterior segment of the left upper lobe removed. The patient responded well until the seventh postoperative day, at which time a spontaneous pneumothorax developed which was asymptomatic. Thoracotomy tube drainage was established for ten days with complete re-expansion of the lung.

CASE 34. J. E. F., an eighteen year old white man, had the apical-posterior segment of the left upper lobe removed. Delayed expansion of the lung developed which was attributed to improper function of the tubes. Treatment consisted of careful observation with achievement of full re-expansion three months after surgery.

CASE 9. W. L. M., a seventeen year old white man, had two anterior subsegments of the left upper lobe removed. Persistent density and fluid accumulation developed at the site of the resected segments which responded well to repeated aspirations with instillation of varidase.®

CASE 24. W. H. M., a sixteen year old Negro boy, had multiple segments removed from the right upper lobe and the right lower lobe. Atelectasis developed followed by a bronchopleural fistula. Despite thoracoplasty intrapleural empyema and fluid accumulations removed. Prior to surgery the patient had a slightly prolonged bleeding and clotting time, and there was persistent oozing after surgery. Hemothorax developed which did not respond to varidase instillation and necessitated decortication. Following this the patient re-

TABLE IV

PRESENT STATUS OF FORTY-EIGHT PATIENTS

Status	Time since Surgery				Total	
	6 Months	6–12 Months	12–18 Months	18–27 Months	Number	Per cent
Well; negative sputum; no active disease..	2	18	9	11	41	83.3
Limited; negative sputum and no active disease.....	..	2	2	1	5	10.4
Under treatment for pulmonary disease; sputum negative.....	..	2	..	1	3	6.2

in the extrapleural space developed. Treatment consisted of thoracoplasty, multiple aspirations and catheter drainage of the extrapleural and intrapleural spaces. Four months after surgery the patient was discharged on bedrest.

CASE 12. H. T., a forty-one year old white man, had segmental resection of the superior segment of the left lower lobe and the lateral basal segment of the left lower lobe. He ran a persistently elevated temperature postoperatively and a fluid air loculation at the site of the resected segment developed with progression to bronchopleural fistula and empyema. Treatment consisted of rib resection and suction-tube drainage of the space. Four months after surgery the patient left the hospital with negative sputums and a healed wound.

CASE 11. C. H., a seventeen year old white boy, had the apical posterior segment of the left upper lobe removed. The patient ran a persistently elevated temperature for eighteen days postoperatively. A bronchopleural fistula developed which did not respond to tube drainage and necessitated thoracoplasty with catheter drainage of the space. Four months after surgery the patient was discharged with negative sputums and healed wound.

CASE 4. J. B. W., a twenty-one year old white man, had the posterior portion of the apicalposterior segment of the left upper lobe sponded fairly well for one week, but then a bronchopleural fistula developed which responded eventually to thoracotomy tube drainage.

Miscellaneous Complications

CASES 47 AND 45. Transient radial nerve paralysis following surgery developed in two patients: A. V. V., a thirty-four year old white woman, and M. L. N., a thirty-nine year old white woman. This was attributed to positioning at the time of surgery and cleared spontaneously under conservative management.

CASE 38. L. W. J., a thirty-five year old, white woman, had persistent hemorrhage from a skin incision which necessitated secondary ligation.

CASE 21. D. T., a twenty-three year old Negro woman, had the apical segment of the right upper lobe removed from beneath the previous thoracoplasty because of a persistent cavity. The patient had persistently positive sputum following surgery attributed to a contralateral cavity. At present the patient is still under treatment for her disease.

CASE 3. J. M., a thirty-nine year old Negro man, had the lingula and portion of the anterior segment of the left upper lobe removed. On the first postoperative day a marked asthmatoid reaction developed which

did not respond to the usual asthmatic-type treatment. For four days the patient was maintained on nasal oxygen, intermittent positive pressure oxygen with isuprel® added, and cortisone. Acute gastric dilatation also developed which responded to gastric suction. At present the patient is under treatment for pulmonary disease, with negative sputum.

In the entire fourteen cases complications which necessitated a secondary operation developed in only four patients. These four plus the one case of postoperative spread gives a total of five patients who actually had a major-type complication. The corrected operative morbidity is approximately 10 per cent.

FOLLOW-UP

The present status of the forty-eight patients is summarized in Table IV.

The follow-up period runs from six months to twenty-seven months.

Of the fourteen patients in whom complications developed (Table III), nine are well with no active disease and negative sputa, three are on limited activity status with negative sputa and no active disease, and two are still under treatment for pulmonary disease, with negative sputa.

SUMMARY AND CONCLUSIONS

1. Fifty consecutive cases of segmental resection for pulmonary tuberculosis have been reviewed and analyzed.

2. There were no deaths, but an over-all morbidity of 28 per cent was experienced with a corrected morbidity of 10 per cent.

3. Preoperative studies including laminagrams and bronchograms are important in accurately localizing the disease.

4. The operation is intricate, requiring meticulous attention to anatomic detail during the dissection and careful placing of the tubes at the time of closure.

5. The patient should have frequent postoperative x-rays to detect early impending complications so that active treatment can be started immediately.

6. Segmental resection is a worth while procedure in carefully selected cases.

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Cancer of the Breast

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LIKE most of you, I was brought up in the tradition that the proper treatment for cancer of the breast, when detected early enough, is radical mastectomy, usually followed by postoperative radiotherapy. However, since some of my patients with cancer of the breast have refused to permit radical mastectomy because they dreaded postoperative lymphedema and arm disability, I employed preoperative radiotherapy of the lymph drainage areas followed by simple mastectomy and postoperative radiotherapy. Already one patient has passed the five-year cure limit and is well and clinically free of recurrence, even though she had enlarged axillary glands at first examination. Another patient, a male upon whom I performed a simple hemimastectomy followed by x-ray therapy, has been well for the past three years. In a case with a large malignant mass occupying about two-thirds of the nipple, I simply removed the mass and involved portion of the nipple and repaired the remainder to make a new, smaller nipple, followed by intensive radiotherapy. This patient is now well and free of recurrence some three years after her limited operation. Two of these patients were stage I cases and one was stage II or III. Because of these unexpectedly good results I became deeply interested in this question, the more so because some of my former radical mastectomy patients complained of postoperative disability.

Ultimate results of treatment in breast cancers, even when these growths are rather superficial and readily palpable, are poor. In fact, Williams and his associates[1] in a statistical study of over 1,000 cases of breast cancer have come to the conclusion that final results seem hardly affected by any treatment whatsoever, whether radical or local.

Although the modern tendency is to perform radical surgery on early cases of cancer, the death rate does not seem to be greatly reduced by modern procedures. In fact, McKinnon[2] believes we have failed in our efforts at cancer control. He reports that in Saskatchewan the death rate from cancer of the breast is about as high as it ever has been, in spite of an intensive educational campaign emphasizing early diagnosis and radical treatment.

For a long time we have known that the surrounding normal tissues offer a varying amount of resistance to these growths and lately it has been shown that hormones might affect the course of the disease.

It has been assumed that the earlier the treatment of cancer of the breast, the higher the rate of cure. Yet a study of the literature shows no diminution in the survival rate when therapy has been delayed. This is noteworthy because the cases treated late are usually of a lower type malignancy. Park and Lees,[3] using the five-year survival rate as an index, conclude that it has not been proved that the survival rate of cancer of the breast is affected by treatment of whatever type and, moreover, that statistics strongly indicate that therapy rarely reduces the incidence of death from metastasis. They believe that treatment may cause a 5 to 10 per cent increase, at the most, in the five-year survival rate.

Keynes,[4] one of the earliest workers in this field who expressed grave disappointment in the low absolute cure rate and the rather high percentage of lymphedema of the arm following radical surgery for breast cancer, in 1922 began an investigation of the value of other forms of therapy. As a result of his studies at St. Bartholomew's Hospital in London, England, Keynes concluded that when metastasis of the axillary lymph nodes is present, dissection of the axilla may result in more harm than good.

Naturally, when the nodes are uninvolved, axillary dissection is unnecessary. In fact, some authorities believe that in removing involved axillary lymph nodes they may open up abnormal lymph channels for metastatic spread, but as Williams et al.[1] explain: "It may not be a question of opening up new pathways as much as the removal of normal pathways, leaving only abnormal ones for dissemination."

Statistics from St. Bartholomew's Hospital[4] on over 1,000 cases show that even in stage I cases distant metastasis had already occurred in 20 to 30 per cent of the patients, and even radical mastectomy (which is much too radical for such cases) would fail to produce a cure in approximately one-third of the patients. In such instances, since we must rely upon effective radiotherapy to destroy the microscopically involved parasternal nodes, axillary nodes, supraclavicular nodes, etc., if any surgery at all is to be performed, I believe simple mastectomy is the procedure of choice.

In stage II cases about two-thirds of the patients had distant metastases irremovable by Halsted's classic radical mastectomy. Hence simple mastectomy plus competent postoperative radiotherapy was the procedure recommended by Keynes.[4] He even recommended simple removal of the tumor from the breast followed by radiotherapy, and claimed the ultimate results were equal to radical mastectomy plus radiotherapy.

A statistical study of the site of the tumor showed that about 30 per cent of the malignant tumors were situated in the medial half of the breast from which region the lymph nodes most apt to be involved are those accompanying the internal mammary artery—the parasternal nodes. These lie outside the limits of Halsted's radical mastectomy. They may be mechanically removed by intrathoracic surgery (ultraradical surgery), but few surgeons are willing to, or even capable of, going to this extreme. The involved parasternal nodes may be destroyed, or at least their growth and spread retarded, by competent radiotherapy—a procedure more commonly acceptable to patient and surgeon alike.

Williams et al.[1] believe that "where efficient radiotherapy is available, radical mastectomy should be abandoned in favor of conservative surgery."

McWhirter[5] states that because 75 per cent of all cases of cancer of the breast coming to the Royal Infirmary in Edinburgh failed to show a five-year survival following radical mastectomy, Edinburgh surgeons decided to explore other means of cure, seeking a more successful procedure. Since it was found that radical mastectomy plus postoperative radiotherapy was followed by many deaths from distant metastases, surgeons began to suspect that dissection of the axilla tended to disseminate the disease. Moreover, if the axillary nodes were not involved, their removal was not indicated. Certainly, it seemed desirable to remove the primary tumor and even part of the pectoralis major muscle if the growth is adherent to its fascia, and no attempt now is made to "clean out" the axilla and its fat—rather, this is treated by radiotherapy, started as soon after the simple mastectomy as possible. The lymph nodes in the supraclavicular region and along the internal mammary artery also require roentgenotherapy. Preoperative x-ray treatment is given with this procedure, rather than following radical operation which requires a longer time for healing; hence less dissemination is likely to occur postoperatively.

Personally, I recommend a limited amount of preoperative radiotherapy to seal off the lymphatics and to prevent any possible dissemination during simple mastectomy; this should be followed by postoperative radiotherapy to effect a cure. Treating cancer by pre- and postoperative radiotherapy and simple mastectomy eliminates the great proportion of cases of arm disability due to lymphedema; in fact this complication occurs in only a few cases, actually in less than 5 per cent.

McWhirter's[5] statistics show that from 1935 to 1940 when the usual procedure was radical mastectomy and postoperative radiotherapy, the five-year survival rate for *all* breast cancers (whether treated or not) was 32.4 per cent; whereas from 1941 to 1945 when simple mastectomy plus postoperative radiotherapy was the routine procedure employed, the five-year survival rate of *all* breast cancers referred to the Royal Infirmary at Edinburgh reached 43.7 per cent. This is a distinct improvement. Hospitalization is shortened and, in general, expense to the patients is lessened. Postoperative pain and disability are also reduced, and patients live longer than after radical mastectomy, with or without postoperative x-ray therapy.

By substituting x-ray therapy of the axilla for surgical dissection, five-year survivals have been greatly increased. To quote from McWhirter,[5] "When radical mastectomy is the only method of treatment available and when *all* cases coming to a large general hospital are taken into account, the five-year survival-rate is unlikely to exceed 25 per cent." With preoperative as well as postoperative radiotherapy plus simple mastectomy, the proce-

dure I now recommend, I believe it is logical to expect an even greater five-year survival rate. Adequate radiotherapy, both pre- and postoperative, is essential. The axillary, supraclavicular and parasternal lymph nodes must be radiated sufficiently, but these details we can safely leave in the hands of a skilled radiotherapist.

When Halsted first devised his radical mastectomy, surgeons thought that in removing the axillary nodes as well as the pectoral muscles they were widely excising the breast cancer, and for a while five-year survivals seemed increasing and local recurrences were considerably diminished. Proponents of radical surgery still believe that the only safe measure for the patient is the mechanical removal of every malignant cell from her body. However, it is not possible for a surgeon to be sure he has done this; he has to resort to the supplemental aid of radiotherapy because of possible involvement of the parasternal nodes or because some cancer cells may have contaminated the wound or may have been left behind.

Some investigators have found that radical mastectomy seems occasionally to accelerate death by way of distant metastases and they speculated that the trauma incident to attempts to "clean out" the axillary nodes and fat "en bloc" may actually have been responsible for a certain amount of dissemination of the malignancy to distant sites, particularly by way of the plexus of valveless veins extending from the coccyx to the cranium. This is a likely possibility in some cases.

Halsted[6] and Handley[7] originally believed that breast cancers spread primarily by way of the lymphatics and therefore the earlier and more radical the operation, the better the expected results. This is not entirely true since many of the very early cases involve cancers of high malignancy that grow and metastasize rapidly. For this reason the earlier cases often have the worst prognosis.

According to Handley about 75 per cent of all patients with cancer in the inner half of the breast have involved parasternal nodes when first diagnosed. When patients have cancer in the outer half of the breast and the axillary nodes are already involved when first seen, the probabilities are that in 30 per cent of such cases the parasternal nodes are likewise involved. The largest node involved of the parasternal chain is usually situated in the second intercostal space and some surgeons explore this area first. If positive evidence of cancer is found there, no other surgery is attempted; the patient is simply given roentgenotherapy. Some surgeons, on the other hand, disagree that evidence of parasternal or supraclavicular or of high (not low) axillary node involvement contraindicates a radical mastectomy.

McKinnon[2] and others are of the opinion that breast cancer is not a local disease and that in fatal cases probably the spread was by way of the blood stream instead of through the lymphatics, and that in such cases the disease spread beyond the confines of the breast; thus surgery would be too late to produce effective results.

Early cases often have the worst prognosis because so many of them have a very high degree of malignancy. Bloom[8] has demonstrated that patients with breast cancers one year old at the time of operation did as well, so far as five-year survivals are concerned, as did the patients who had breast cancers only one-half year or less prior to surgery.

Long survival after surgery is not proof of the operation's effectiveness, for many patients with untreated breast cancer live just as long. It is suggested that the probable explanation of long life in both treated and untreated cases lies in the fact that growth of the cancer was slow and metastasis was very late. Therefore, many authorities[9] believe that a palliative operation, such as simple resection of the tumor or a simple mastectomy, is desirable, whereas a radical mastectomy often is not, especially since survival rates after simple or radical mastectomy, or irradiation alone, are virtually equal.

In patients with axillary involvement, recent authorities have been recommending extension of the Halsted radical operation to include removal of the supraclavicular nodes (which usually occur secondary to axillary node involvement) and the parasternal nodes. Statistics show that in patients with axillary involvement 52 per cent have had positive malignancy in the parasternal nodes and 9 per cent have had malignant involvement of the supraclavicular glands, yet the old Halsted "radical mastectomy" is still being performed as the most efficient operation for breast cancer. Obviously, it can only be of value when the cancer is still confined to the breast, without

spread either by way of the lymphatics or the blood stream. It is in just such cases that we believe simple mastectomy is the only surgery indicated or justified. Of course, roentgen therapy is advisable in all cases, since microscopic involvement of the axillary, the supraclavicular and/or the parasternal nodes, may be present. This is more evident when the primary breast lesion is located internal to the nipple line. Recent studies of MacDonald et al.[10] confirm suspicions formerly held by many that, while it is true that the supraclavicular node involvement is secondary to axillary involvement and may be present even though the supraclavicular nodes are clinically normal, the parasternal node involvement is a primary one (as is the axillary) and often even antedates spread to the axillary nodes. It is little wonder, therefore, that the classic Halsted mastectomy (unaccompanied by roentgen therapy) is followed by poor results in many cases. If the glands are radiosensitive, then pre- or postoperative roentgen therapy can favorably affect these nodes which are not removed by the Halsted radical mastectomy. The point I wish to emphasize is that it is logical to think that equally good results (without mutilation and without disability due to lymphedema of the arm) are possible with simple mastectomy plus roentgen therapy. Moreover, I believe that this therapy is equally as good in advanced as in early cases of breast cancer.

Wangensteen's statistics[11] show that 65 per cent of all patients with axillary involvement also have involvement of the nodes in the supraclavicular triangle of the neck, or in the nodes alongside the internal mammary artery. He therefore has devised an "ultraradical mastectomy" with excision of all the structures included in Halsted's radical mastectomy plus removal of the nodes in the supraclavicular and parasternal regions. Andreassen and colleagues[13] also have recently extended the radical Halsted operation to include removal of the supraclavicular and the parasternal nodes. This is indeed extensive surgery; vastly superior results will have to be demonstrated before this procedure can be recommended to all surgeons. For men like Wangensteen, this operation may yield superior results but for the average general surgeon it seems much too extensive. Extensions to the classic Halsted radical mastectomy have also been devised by Margottini and Bucalossi,[15] and by Urban.[16] Probably Urban's procedure is the most popular.

I prefer to depend upon pre- and postoperative radiotherapy to take care of the lymph drainage areas, with simple mastectomy to remove the primary growth. Besides, the vast majority of patients will much prefer radiotherapy alone, or combined with simple mastectomy.

Naturally, statistics vary. For instance, Handley[12] demonstrated that the parasternal glands are also involved in almost 50 per cent of cases of breast cancer. He found, also, that distant metastases (blood-borne) may even have antedated diagnosis and treatment. For this reason the mortality rate from breast cancer in women aged thirty to sixty still remains high. It has been demonstrated repeatedly that breast cancers can spread by way of the blood vessels, although some authorities are still convinced that the early spread is through the lymphatics and that the axillary ones are the first involved. It was only on this premise that Halsted was justified in advising radical mastectomy as the preferred treatment. If early breast cancers spread embolically through the blood vessels, then the Halsted operation is of little avail and in performing it we would be simply mutilating a patient who has metastasis beyond the limits of Halsted's radical mastectomy. For many years surgeons suspected that some of the spread was by way of the parasternal nodes. In fact in 1949 Handley and Thackray[12] showed that about one-third of the patients subjected to radical mastectomy already had carcinomatous involvement of the parasternal nodes along the internal mammary artery; five years later they found this fact to be true even in a greater proportion of cases. In addition, Andreassen, Dahl-Iversen and Sorensen[13] found that one-sixth of the patients with axillary node involvement also had involvement of the supraclavicular nodes (which are not removed in the classic radical mastectomy of Halsted). But, perhaps more significantly, Gatch and Culbertson[14] have recently demonstrated that probably in most cases metastases occur by embolism through the blood stream, so that often when an "early" case is presented for surgery, it is already inoperable because distant metastases are present, although undetectable, and retrosternal in-

volvement of the lymph nodes likewise may be present. In such cases, longevity is not promoted by any surgical operation; only radiotherapy, with or without a simple mastectomy to remove the primary growth, can retard the natural evolution of the malignancy, provided it is radiosensitive.

Even if radical mastectomy plus radiotherapy did produce a slightly higher incidence of five- and ten-year cases, investigators doubt that this radical procedure can be justified; certainly, length of life should not be the only criterion to affect our judgment in these cases, since in some instances patients may prefer to live a year or two less rather than submit to a mutilating, possibly disabling, operation.

To repeat, I have objected to the deformity and disability resulting from radical mastectomy. Perhaps the incidence of postoperative lymphedema of the arm in my own cases is too high. At any rate, I have been impressed with statistics indicating that therapy seems to have little effect upon mortality from breast cancer. Several clinics have compared treated with untreated cases and have concluded there is little evidence that therapy prolongs life. If so, why subject these patients to mutilating operations that often cause disability throughout the rest of their lives? I am impressed with McWhirter's[17] opinion that simple mastectomy and radiotherapy is probably the best procedure to adopt in the average case. I would prefer part of the radiotherapy preoperatively rather than exclusively postoperatively, following this with simple mastectomy, especially if there is clinical evidence that roentgenotherapy has caused the enlarged axillary lymph nodes to become smaller and softer. The radiotherapy is completed in the postoperative period. Otherwise radical mastectomy is indicated, although the probabilities are that the surgery will be ineffectual so far as longevity is concerned.

One factor emphasized by Gatch and Culbertson[14] is the importance of the surrounding normal tissues in retarding spread or growth of the cancer; in fact, spontaneous cure of a cancer may occasionally be explained by this process.

Frozen-section biopsy of the primary tumor or of an involved node should first be done for diagnostic purposes. McWhirter's therapeutic procedure of simple mastectomy and then intensive radiotherapy is adopted, or radiotherapy alone is used. In addition, a preoperative lung and bone x-ray survey is needed to rule out possible metastasis. X-rays of the skull and extremities may be omitted from this routine survey, unless clinical symptoms suggest their inclusion, since the incidence of their involvement is small.

In stage I cases in which the tumor is apparently confined to the breast, although some authorities prefer to do the radical Halsted operation, McWhirter's statistics indicate that he obtains equally good results with simple mastectomy followed by high-dosage postoperative radiotherapy.

In stage II lesions, in which both the primary breast tumor and the involved axillary lymph nodes are mobile, most authorities agree that Halsted's radical mastectomy followed by postoperative radiotherapy, is the preferable procedure. Yet if the glands diminish in size and soften under preoperative radiotherapy, I believe this is an indication that they are radiosensitive and that probably in such cases equally good results may be obtained by following radiotherapy with simple mastectomy (McWhirter's procedure in reverse).

In stage III lesions when examination shows extensive involvement of surrounding tissues and when the breast tumor is associated with fixed lymph node metastasis in the axilla or with parasternal lymph node involvement (as proved by biopsy) or with skin involvement, etc., most surgeons think that radiotherapy alone is indicated. About one-third of such patients will exhibit good results.[18] However, I think it of value (cosmetically and otherwise) to remove the primary growth by simple mastectomy. Use of the radical operation and postoperative radiotherapy in these advanced cases results in a higher percentage of postoperative or postradiotherapy lymphedema without increasing longevity.

McWhirter's procedure has produced better results in a large series of cases (up to ten years postoperatively in stage I and II cases) than were produced by his colleagues using radical mastectomy. In fact, investigators who studied these results concluded that McWhirter's procedure produced as good results after five years, considering all cases, as were produced by radical mastectomy with or without radiation.[19] McWhirter's figures[5] show that 42 per cent of the patients were alive five

years following use of his technic as compared with only 31 per cent in patients having radical mastectomy plus postoperative radiotherapy; at ten years, 15 per cent of his patients were alive, compared to 18 per cent of patients treated by radical mastectomy and postoperative radiotherapy. The advantages claimed for the McWhirter procedure are: (1) There is less surgical shock and operative morbidity, and less cancer dissemination, because one avoids the prolonged dissection and manipulation of tissues that the radical operation requires. (2) The radiotherapy is simpler and there is virtually no lymphedema and postoperative disability of the arm as compared with 10 to 70 per cent lymphedema of the arm after radical procedures. (3) Hospitalization is shorter and the patient is able to resume work more promptly. There are two notable contraindications to using McWhirter's procedure, namely, excessive obesity and old tuberculosis in upper lobe of a lung. In such instances radical surgery is advisable. Even if a breast cancer develops during pregnancy or lactation, while the prognosis is worsened, with the McWhirter procedure 31 per cent were alive five years later, whereas none treated by radical surgery lived for five years.

According to Ash et al.[20] preoperative radiation may be expected to sterilize the axilla in only about one-third of the cases—apparently the remaining cases are less radiosensitive because during subsequent surgery living cancer cells were found. In Ash's series, after preoperative radiotherapy, a simple mastectomy was done in twenty-six cases and in six of these there was recurrence, whereas in forty-eight similar cases with preoperative radiotherapy there were only three cases of recurrence following radical mastectomy. These figures argue against McWhirter's procedure. Sterilization and hormone therapy, of course, are often indicated as supplemental therapy.

Thayssen[21] shows that x-ray castration is distinctly beneficial in cases of breast cancer with metastasis. Even among patients treated by radical surgery with postoperative radiotherapy, if no castration was done all these patients were dead in five years; whereas with additional x-ray castration (which is especially important in patients under forty-five with osseous lesions) the results are as good as with surgical castration. I believe that x-ray castration should be done on all such patients still menstruating. Radiologists suggest that after the menopause this procedure is unnecessary.

After any type of operation, if recurrence takes place (especially in the bones), radiotherapy is recommended. This procedure is also used with or without local excision when skin or lymph nodes present localized recurrences. When radiotherapy cannot be given or has already been given and further treatments are not indicated, then steroid hormone therapy can be tried. In patients up to the age of forty-five most authorities use the male hormone, but in older women they prefer the female hormone. To these older women some authorities give the male hormone if metastasis of the bone is present, and the female hormones for the treatment of metastasis of soft tissues. If one type of hormone after several months' trial seems no longer efficacious in retarding the progress of the disease, one may switch over with benefit to the opposite hormone.

Garland's[22] analysis of the results of 100 consecutive cases of primary breast cancer in two separate hospitals in San Francisco, most of them treated by radical mastectomy with or without radiotherapy, in general showed results inferior to those reported by McWhirter in which he used simple mastectomy plus vigorous postoperative radiotherapy. We may therefore conclude that the McWhirter procedure is the method of choice, especially when supplemented by x-ray castration in menstruating women.

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The Use of Clorpactin WCS 90 As an Antiseptic in Surgery

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THE medical profession is perpetually searching for the ideal antiseptic. In spite of the numerous preparations available, there are none that can qualify as the ideal antiseptic. What is an ideal antiseptic? It is probably a solution which has a complete germicidal action against all bacteria but at the same time is harmless to the tissues of the host. The preparation should be simple. It should be readily prepared, easily applied and stable at room temperatures.

A preparation based on a modified buffered hypochlorous acid derivative which tends toward meeting these requirements is a product known as Clorpactin WCS 90,* a brand of monoxychlorosene. The product is a water-soluble powder whose dilute solutions are powerfully germicidal, fungicidal and virucidal, yet appears to be non-toxic and non-irritating to the host tissues. It is a fairly free-flowing white powder of an apparent specific gravity of approximately 1.2. The pH of a 0.25 per cent solution at 18°c. is 6.8 to 6.9. The average active chlorine content ranges from about 3.5 to 4 per cent. It is interesting to note the pronounced wetting and penetrating properties of Clorpactin WCS 90 in as dilute a solution as 0.25 per cent. There is a sharp increase in these properties in greater concentrations.

For general application, a 0.25 per cent solution by weight of Clorpactin (2.5 gm./L.) in lukewarm tap water is the most desirable concentration. As stronger solutions are greater oxidizers, a 0.5 per cent solution may be used for treatment of conditions in which considerable amounts of organic debris are present.

The solution is prepared quite readily by stirring the desired amount of the powder into lukewarm tap water, in a glass, ceramic or enameled receptacle. A few minutes of this vigorous stirring is all that is necessary. The initial solution will appear cloudy with a foamy top. In a few minutes the solution will clear but the characteristic foam will remain on top. A faint odor of hypochlorous acid is present. The taste is that of hypochlorous acid which is somewhat reminiscent of hydrogen peroxide. The solution should be made up fresh if possible. Although the solution prepared as heretofore shown retains a large percentage of its potency for a normal eight-hour day, the most effective results can be obtained from the highest potency which characterizes fresh solutions.

The germicidal spectrum of Clorpactin WCS 90 is an extremely broad one. It has powerfully fungicidal and virucidal properties as well as being an excellent deodorizer. The phenol coefficient is 27 when tested against Eberthella typhosa by the F.D.A. method. Five cubic centimeters of 0.28 per cent solution will kill 0.5 cc. of a five-day broth culture of the spores of Clostridium tetani in five minutes at room temperature. Guinea pigs that had been inoculated with a heavy suspension of living virulent human tubercle bacilli (H37 Rv strain) which had been in contact with a 0.5 per cent solution of Clorpactin WCS 90 for one minute showed no evidence of tuberculous diseases when killed seventy days later. One cubic centimeter of a 0.28 per cent suspension of Clorpactin WCS 90 in common salt was added to a 0.5 cc. suspension of rabies virus, and 0.3 cc. of this mixture was injected intracranially in each of several rats. All of the controls died of rabies, but all of the rats injected with the solution containing the product lived. The same results were obtained with both Flury rabies virus and Pasteur rabies virus. In dilutions as great as 1:12,000 there was no growth of Endamoeba histolytica culture after forty-eight hours. The fungicidal effect on various samples of yeast of the

* Manufactured by the Guardian Chemical Corp., Long Island City, N. Y.

genera cryptococcus, saccharomyces and candida is similarly profound.

A list of bacteria tested by the Department of Microbiology and Immunology of the Faculty of Medicine of the University of Sao Paulo[1] in which Clorpactin WCS 90 has excellent bactericidal effect is as follows: Streptococcus pyogenes, Bacillus anthracis, Corynebacterium diphtheriae, salmonella, shigella, Proteus vulgaris, brucella, Aerobacter aerogenes, Serratia marcesens, Pseudomonas aeruginosa, Klebsiella pneumoniae, Pasteurella pestis, Hemophilus pertussis, Vibrio comma, Streptococcus faecalis, Paracolobactrum intermedium, Escherichia coli and Shigella dysenteriae.

Elsewhere, this same product was shown to have a bactericidal action against Ps. aeruginosa (Bacillus pyocyaneus), Bacillus subtilis and Pr. vulgaris. Comparative studies were made of the more accepted treatment of infections of Ps. aeruginosa with dilute solutions of acetic acid against dilute solutions of Clorpactin WCS 90. A control solution of 938,000 bacteria per ml. (average) was used; 0.5 cc. samples were treated with 1:500 solution of Clorpactin WCS 90 for one and a half minutes and cultured on nutrient agar. The result showed that the solution reduced the organisms 100 per cent. Even at a concentration of 1:5,000, the reduction was 99.96 per cent.

Actually, the destruction of any simple organism as Staphylococcus aureus takes place in a matter of seconds. A few seconds' contact time against a culture of Staph. aureus containing 100,000 organisms is sufficient to reduce the count to zero.

General toxicity was studied by intravenous injection, intradermal injection, intraperitoneal injection and feeding. Solutions of 0.28 per cent injected intravenously and intraperitoneally were without effect and all mice were alive and well for seventy-two hours. There was no irritation on intradermal injection. When test animals were fed with a 0.28 per cent aqueous solution along with the regular food and water, they were normal throughout the period and gained more weight than the control animals.

Skin toxicity tests of both the acute and subacute types were made in rabbits. The method used was the procedure described by Draize et al.[2] in which an area of skin was abraded in one group of animals, while in the second group the skin remained intact. Each group was equally divided and treated with two concentrations of Clorpactin WCS 90 in a concentration of 0.28 and 0.56 per cent, respectively. The rabbits exhibited no detrimental systemic effects. The behavior and appearance were normal and all gained weight after treatment.

Allergenicity tests were made in twelve guinea pigs according to the procedure employed by Draize. The absence of a reaction at the test sites and of flare-ups at the sensitizing sites permits the conclusion that the test animals did not develop sensitivity to Clorpactin WCS 90. The irritating effect of the product on mucous membranes was studied by instilling some 0.25 per cent aqueous solution into the conjunctival sacs in one eye of each of six rabbits. The irritation was rated according to the method of Draize and Kelly[3] in which the maximum score per rabbit is 110. Four rabbits had ratings of two in the test eyes one hour after instillation and 0 for all successive readings. The other two rabbits showed no irritation at any time. Patch tests of 0.25 per cent solution on humans were negative, indicating that neither primary skin irritants nor cutaneous sensitizers are present. Little or no irritation is complained of subjectively when applied to a denuded area other than the initial stinging or tingling noticed on application.

The speed of its germicidal action and the completeness of the spectrum, with the absence of toxicity, irritation or sensitization, bring Clorpactin close to the goal of the ideal antiseptic for preoperative skin preparation. The skin may be cleansed with any soap preparation to remove the surface oils if desired although one may rely upon the detergency of the solution alone. A 0.25 per cent aqueous solution of Clorpactin WCS 90 is applied liberally to the operative site and the contiguous area. Hair-bearing areas that may be involved are satisfactorily sterilized with this solution.

The postoperative dressing of the incision is gauze soaked with 0.25 per cent aqueous solution of the product. Its use is particularly advantageous in pedicle grafts where an infection by the contaminant group of organisms occurs so frequently. The wet dressing not only protects the operative site through the critical period but also serves as a deodorant. A small plastic tube incorporated in the dressing

will permit fresh antiseptic solution to be introduced even when a plaster cast fixation is used.

A series of 164 surgical procedures have been performed using a 0.25 per cent aqueous solution of Clorpactin WCS 90 for pre- and postoperative antisepsis. The breakdown of cases appears in Table 1.

TABLE 1

Procedure	No.
Tubed pedicle grafts	4
Flap pedicle graft	2
Skin graft	6
Rhytidoplasty	4
Rhinoplasty	10
Mammaplasty	2
Cleft lip, repair of	4
Cleft palate, repair of	6
Otoplasty	2
Excision of surface tumors	57
Reconstruction of digits	3
Reconstruction of scars	21
Surgical abrasion of face	43
Total	164

Although surface infections are not a usual feature in these types of cases other than the pedicle grafts, irrespective of the antiseptic solution employed, there are certain minor annoyances which do occur, such as minute collections of purulent material about the sutures. These have not been evident with Clorpactin antisepsis. The freedom of infection and odor in cases of pedicle grafts are phenomenal; however, the use of the antiseptic must be continued throughout the healing period. Its value is similar in skin grafting also. Ps. aeruginosa (B. pyocyaneus) infections do not occur.

Some caution must be used, however, in sterilizing metallic instruments with solutions prepared with Clorpactin WCS 90 because of the possibility of oxidation of the metal. While stainless steel and chrome-plated instruments are not affected, uncoated steel such as scalpel blades blacken almost instantly. Plastic, rubber, nylon and many other synthetic materials are unaffected. It should be pointed out that the potency of prepared solutions of this product decrease upon standing, even at room temperature, and it is necessary to prepare a fresh solution as often as every eight hours. Although the use of this antiseptic solution in an operating room where many cases are handled make this objection very minimal, its use in the individual case does mean a few minutes spent preparing the solution. The author believes that this is not a hardship. It can be done by the most inexperienced of the operating personnel, for the toxicity is so low even an inaccurately prepared solution is not dangerous to anything other than the bacteria.

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Control of Postpartum Lochia with Kutapressin

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LOCHIA[1] is a vaginal discharge which occurs during and the first week after childbirth. Lochia cruenta or rubra, a reddish or sanguineous discharge, is present for about one week following delivery. Lochia alba, a whitish discharge, usually follows lochia cruenta and is present for about another week or more.

Numerous inquiries were made among our colleagues, locally and elsewhere, to obtain their opinions on the length of time lochia was present in their patients. No agreement was obtained from their answers. Some clinicians stated that in their patients lochias of all the various types occurred from three to as long as six weeks following delivery. However, the majority of doctors interrogated reported that lochias lasted for about one month following delivery. These reports were in accord with our own findings.

Benedek[2] reported most lochias under physiologic conditions were not bloody red beyond the eighth to tenth day, except when the patients got out of bed for the first time. He quoted Pankow who found that in a series of 704 obstetric cases many patients in the uncomplicated group exhibited blood-tinged lochia for as long as six to eight weeks following delivery.

We were interested also in the effect, if any, which lactation had on the involution of the uterus. It is accepted that lochial discharge is related to uterine involution.

Upon review of Benedek's notable article[2] the conclusion drawn was that without lactation the duration of bloody lochia is prolonged; this confirms earlier findings regarding the favorable effect of lactation on uterine involution. However, the Bernstines[3] found that the average discharge per pad was greater among nursing mothers than among those receiving stilbestrol and not nursing. These observers[3] found that the average lochial discharge per pad was much less at night than during the day when the patient was more active. Zummo and Rudolph[4] reported that ambulatory patients did not always reveal an increase in the amount of lochia. Rotstein[5] found that his patients who were out of bed on the third or fourth postpartum day exhibited a more profuse lochia which is to be expected since by standing or sitting upright the flow of lochia is helped by gravity.

The suppression of lochia should be differentiated from lochiometra, which is the term for the retention of lochia in the uterine cavity as indicated by diminution or complete absence of external lochial discharge. Lavarello[6] claimed that vesicle hyperdistention, uterine atonia and spasm of the internal orifice of the uterus caused retention of lochia.

Heffernan and Sullivan[7] reported a case which featured complete absence of lochia in a primigravida who underwent a cesarian section four weeks before term.

Our interest in the control of lochia arose from the previous work of one of us (W. M.)[8] in which it was reported that cutaneous surgical wounds seemed to heal better when vasoconstrictive measures were employed. It was noted also that the tissue edema of first and second degree burns appeared to impede recovery.[9] On several occasions (unpublished data) it was observed that during cesarian section bleeding was lessened when the patients were treated preoperatively with a vasoconstricting substance (kutapressin®*). Comparable observations had been recorded by Holtman in dental surgery.[10]

Hence it was thought that uterine involution, with the control of lochial discharge, might be affected favorably if a non-toxic vasoconstricting medication were to be employed

* Kutapressin is a non-toxic and non-allergic selective vasoconstricting principle isolated from liver. It is manufactured by the Kremers-Urban Company, Milwaukee, Wisconsin.

postpartum. Lochial discharge contains marked amounts of blood. Hence measures which would assist nature in retaining this precious material would help to prevent morbidity and assist in adequate recovery.

Numerous postpartum patients of other attending physicians were used as controls. These ward patients were in the same rooms with the experimental group. All received similar food and care. Thus it was easy to compare the degree of lochia daily and the period of time required for its control in both the experimental group and the control group, who received no vasoconstrictive measures for lochial control.

Both the experimental and control group left the hospital on various postpartum days. All of the control patients still had various degrees of lochial discharge. However, the experimental group exhibited a marked difference from the control group.

METHOD OF TREATMENT

Patients were placed in the experimental group as they presented themselves. Included in this group were primigravidas and various types of multiparas. Ages ranged between sixteen and forty-one years. Some patients in the experimental group had episiotomies, and many of the deliveries were with low forceps.

However, all patients in the experimental group received $\frac{1}{320}$ gr. of ergotrate® intragluteally immediately after the placenta was delivered. Each patient was then given 2 cc. of kutapressin subcutaneously each day during the hospital stay. No other medications were employed. The control group of patients received no kutapressin but were given varying doses of oxytocic preparations orally or parenterally several times during the first day according to routine orders of their attending obstetricians.

Patients in both groups became ambulatory within three days following delivery. About one-third of the patients in both groups nursed their babies, while those patients who did not were given stilbestrol orally.

EXPERIMENTAL RESULTS

There were sixty-eight consecutive cases in the experimental group, thirty-four requiring low forceps delivery. Each patient in this group received daily 2 cc. of kutapressin parenterally (most by the subcutaneous route). No perceptible difference in the postpartum discharges of the experimental (kutapressin) and the control group was noted on the *first day*. However, on the *second day* the experimental group showed an orange-colored serous discharge. This discharge became light pink on the *third day* and on the *fourth day* was diminished and orange-tinged. By the *fifth day* the discharge was scant, serous and clear colored. Cessation of all lochial discharges was noted by the *sixth day*. Uterine involution seemed to keep pace with this cessation of lochial discharge.

No side reactions of any sort were noted from this experiment. As a matter of fact no known adverse reactions have been recorded with the use of kutapressin. All patients tolerated the parenteral injections very well, there being little pain and no sore or swollen arms after injection. No elevations in blood pressure occurred.

Furthermore those patients in the experimental group appeared to receive an added stimulus from this therapy around the third postpartum day. Nursing mothers who had not been given stilbestrol to dry their breasts seemed to exhibit a decided and increased lactogenic response. The supply of milk was greater and more rapid.

Four cases in the experimental (kutapressin) group complained of a recurring slight serosanguineous vaginal discharge between the second and third postpartum weeks. Several injections subcutaneously of kutapressin daily (2 cc.) completely suppressed further lochial discharge. Two patients reported that they passed small blood clots, but no further discharges were reported.

The control group of patients retained their lochial discharges up to two weeks or more after delivery.

COMMENTS ON THERAPEUTIC RESULTS

As for the reasons for evolving this new postpartum therapeutic procedure, we have been told by our patients that they prefer to have the time of their postpartum discharges shortened, although the procedure is more costly. Taber[11] points out that "these foul-smelling odors are presumed to arise from the chemical and bacterial decomposition of blood and cellular debris." Therefore, since the average woman is fastidious, particularly postpartum

when this offensive discharge is present, its accelerated eradication is indeed welcomed.

Then too, patients prefer not to have to wear perineal pads because of this discharge. Furthermore, and perhaps more important, the rapid termination of this postpartum discharge conserves the blood elements which are lost when lochias are present for several weeks or longer. The mere fact of protein conservation seems to aid or even foster a better lactogenic response in those patients who nurse their offspring under kutapressin therapy.

Besides the suppression of lochial discharge, there is another advantage which has to do with more rapid uterine involution. It appears that the rapid suppression of lochias is related directly to rapid uterine involution when such patients are given the benefit of kutapressin therapy.

SUMMARY

1. Kutapressin, a new non-toxic selective vasoconstrictor, was successfully used in sixty-eight consecutive postpartum cases to suppress lochial discharges. By the sixth postpartum day, the lochial discharges were eliminated.

2. A daily parenteral injection of 2 cc. of kutapressin was administered to each patient during the hospital stay.

3. Uterine involution appeared to keep pace with lochial control under this therapy.

4. A definite increased lactogenic response was noted in those mothers who were nursing their offspring under kutapressin therapy.

5. Those postpartum patients who did not receive kutapressin therapy (control group) showed no similar findings.

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BRONCHOPULMONARY DISEASES—
SYSTEMIC DISEASES, FUNGOUS
INFECTIONS, PNEUMOCONIOSES

Pulmonary Manifestations of Systemic Diseases*

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ROUTINE x-rays of the chest of apparently healthy individuals are a constant reminder that a "silent" chest does not necessarily contain healthy lungs and that a "noisy" chest need not connote serious disease. The presence or absence of the latter can be established only by a chest x-ray, the findings viewed in the light of the patient's history, physical signs and pertinent laboratory tests. Occasionally x-ray of the chest reveals abnormal markings of a type and distribution which are suggestive of being the manifestations of a systemic disease. In such, the chest x-ray may be the first to draw attention to the presence of a widespread disturbance which might otherwise escape detection. Or else, the information obtained may be of additional help in differential diagnosis. In either case the lung may serve as a mirror of what is going on in organs and tissues of the body not accessible to direct examination.

Although roentgenography and its various modalities occupy a key position in chest diagnosis, it would be foolhardy to minimize the value of other means of investigation. A history obtained by the physician, a thorough physical examination and the necessary laboratory tests, including bronchoscopy and, when indicated, exploratory thoracotomy for the obtainment of a biopsy specimen, are as essential in arriving at a diagnosis as are the roentgen findings. In fact, there are occasions when the physical examination is more informative than the chest x-ray findings and the history superior to both. In the diagnosis of obscure systemic disease with pulmonary manifestations, one may have to resort to all possible diagnostic tests and the true nature of the condition may still remain unknown.

Insofar as roentgen diagnosis *per se* is concerned, there is nothing pathognomonic about lights and shadows in a chest x-ray. An area of density may represent consolidation caused by neoplasm, pneumonia, tuberculosis or a transient atelectasis caused by temporary obstruction of a bronchus. A circumscribed area of translucency may represent a cavity caused by abscess, tuberculosis, neoplasm or lung cyst. The abnormal roentgen markings assume added significance when viewed on a background of what the physician knows of the patient's family and personal histories, occupation, travels, as well as the physical and laboratory findings. The black and white shadows then assume various shadings. With experience the presence of a particular disease may be suspected or made with a reasonable degree of accuracy on the basis of the roentgen findings alone but a definitive diagnosis requires confirmatory evidence.

Broadly speaking, disease affecting the lungs and appendages may be grouped into one of three major categories: (1) Primary diseases which include developmental defects, new growths, traumatic injuries and similar conditions. The majority of the acute bacterial and viral pneumonias, pulmonary suppurations, benign and malignant neoplasms and tuberculosis exemplify this group. (2) Secondary dis-

* Excerpts from a book entitled, "The Lung as a Mirror of Systemic Disease," to be published by Charles C Thomas, Springfield, Ill.

eases which include pulmonary emboli, metastatic malignancies and, so-called, "terminal" pneumonias. (3) Concomitant diseases in which the respiratory tract is involved either initially or in the course of systemic diseases as an active, more or less, co-equal participant. The present discussion will deal with the last-mentioned. Some of the conditions to be discussed are infrequent; several are rare. But it is well to bear in mind that a rarity once recognized often becomes commonplace. Furthermore, for every patient with an unusual or bizarre condition discovered in specialty practice, many times the number pass through the offices of physicians and hospital wards with the disease either unrecognized or misdiagnosed.

The order in which the diseases will be presented in the following pages is arranged primarily for orientation purposes, not as a classification in the generally accepted sense of the term since it is impossible to draw sharp nosologic distinctions between one group of diseases and another. This applies especially to diseases of the skin and allergic diseases or to the latter and disturbances of metabolism and certain blood dyscrasias. Several of the conditions to be mentioned cannot be fitted at present into any classification because they are too fluid to be pigeonholed into specific compartments. This is due to lack of knowledge of the cause. With the development of new modalities in diagnosis and treatment, diseases and syndromes are constantly being discovered, more often rediscovered, and new ones are being created.

GENERAL CONSIDERATIONS

When the lungs are involved as part of a systemic disease, the following are noteworthy: (1) a symmetric distribution of lesions in both organs; (2) a vascular or perivascular pattern of abnormal lung markings, and (3) a tendency toward pleural implication. The first and second elements are related to the fact that the pulmonary involvement in most systemic diseases is either within or along blood vessels and/or lymphatics. The third is due to the fact that the pleura is richly supplied with blood vessels and lymphatics. Furthermore, in man, the blood vessels supplying the pleura, as well as the stroma of the lungs, are bronchial arteries, tributaries of the aorta and therefore of the systemic circulation.

The pulmonary changes giving rise to abnormal roentgen patterns are a composite of (1) "normal" bronchovascular markings varying with the age, sex, occupation and body build of the individual, also the conditions under which the roentgen examination is made; (2) physiologic and pathologic changes within the air-containing and/or fluid-containing units of the lungs which determine to a large extent the radiotranslucency of the affected parts, and (3) the dissolution of the normal architecture of the lung by fibrosis, emphysema, consolidation or necrosis, also the associated reactions in pleura, lymph nodes and adjacent structures. *In toto*, these several components endow the lights and shadows in the chest x-ray with certain qualitative and quantitative distinctions which immediately bring to mind certain possibilities to be considered in differential diagnosis.

A disease may manifest itself in the lungs in diverse manner and dissimilar diseases in comparable manner. The pulmonary changes may assume the configuration of a diffuse network of delicate or coarse striations; small or large air cysts, miliary or nodular infiltrations, patchy or massive consolidations with or without an associated adenopathy and pleuritis; often there is a combination of the aforementioned. Nevertheless, these several patterns may be the result of a single or a limited number of agents. On the other hand, diffuse interstitial changes in the lungs may result from viral pneumonia, sarcoidosis, rheumatoid disease, scleroderma, chronic pulmonary congestion and a host of other conditions. A cystic lung may be associated with pituitary disease, histiocytosis, tuberous sclerosis and other conditions to be mentioned later. At least fifty abnormal states may give rise to miliary or nodular pulmonary infiltrates. It would take us far afield to enumerate the diseases which may give rise to pulmonary consolidation and/or pleural effusion. The totality of the chest x-ray findings depends on the type and extent of tissue involvement as well as the duration and intensity of the disease. As the morbid state progresses, or becomes chronic and recrudescent, the causative agent plays an increasingly less important role insofar as determining the roentgen picture as visualized in the chest x-ray.

In the space available it will be possible to present, in outline form, a limited number of

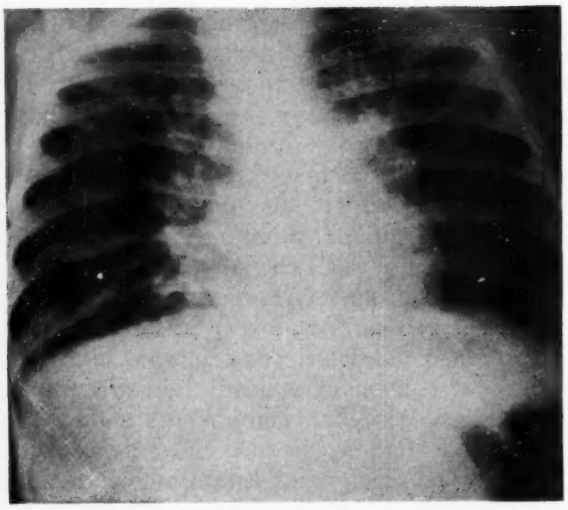

FIG. 1. Cystic fibrosis of the pancreas and pulmonary infection. Chest x-ray showing diffuse linear markings throughout both lung fields. (History of repeated respiratory infections since age of seven months, cough, vomiting, lack of gain in weight; large, loose, yellowish, malodorous stools; pancreatic disease suspected; died at age of 26 months; autopsy showed cystic fibrosis of pancreas, also diffuse fibrosis and bronchiectasis of both lungs.)

systemic diseases which may be associated with pulmonary lesions and to describe briefly the more important ones.

DISEASES OF METABOLISM

Metabolic diseases may affect the lungs through structural damage of the organs and by providing conditions favoring infection.

Pulmonary Infection in the Diabetic. In the presence of diabetes pulmonary infection is apt to be acute and massive, the involved tissues undergoing necrosis and suppuration in a relatively short time. In an elderly person in whom one might expect an apical fibroid tuberculosis, the discovery of a pneumonic or caseocavernous disease may be sufficiently impressive to prompt the physician to examine the patient for the presence of diabetes if the existence of the latter is not already known. Although much of the dread associated with pulmonary infection in the presence of diabetes has been greatly reduced since the introduction of antimicrobial agents, the occurrence of suppurative bronchopneumonia, lung abscess, fungous infection or tuberculosis continue to be serious hazards.

Cystic Fibrosis of the Pancreas. Fibrocystic disease of the pancreas is so often associated with pulmonary infection that the latter is almost an integral part of the syndrome. In fact, the mother may consult the physician because the child had developed an intractable cough rather than because of unmanageable gastrointestinal symptoms or loss of weight. The changes in the lungs are due to obstruction of bronchi by viscid secretion. Early in the disease the chest x-ray may show few abnormalities. After recurring infections, the lungs reveal accentuated perivascular and peribronchial markings affecting chiefly the inner portions of the organs. Later there is increasing emphysema, patchy atelectasis, consolidation and bronchiectasis. Such roentgen findings in an infant are occasionally sufficiently suggestive in themselves to make one suspect the presence of cystic fibrosis of the pancreas. (Fig. 1.)

Histiocytosis. Among diseases of the histiocytic system, two major disorders are recognized, one metabolic and the other inflammatory. The metabolic histiocytoses (Gaucher's disease; Niemann-Pick disease) are heredofamilial conditions characterized by the deposition of specific lipids in the reticuloendothelial cells. On rare occasion the lungs may also be involved, the chest x-rays showing enlarged hilar lymph nodes or miliary infiltrations or both. The inflammatory disorders include Hand-Schüller-Christian disease, Letterer-Siewe disease and eosinophilic granuloma of bone. The pulmonary manifestations of these conditions serve, in a way, to highlight the unified nature of the disorder since comparable changes are met in the several conditions mentioned and frequently they overlap. The pulmonary lesions may take the form of miliary infiltrations, cystic or "honeycomb" lungs, diffuse interstitial fibrosis or localized granulomas. Spontaneous pneumothorax is a frequent complication of cystic lung; chronic cor pulmonale is often encountered in long-standing pulmonary fibrosis. (Fig. 2.)

Amyloidosis of the Lungs. Primary amyloidosis occasionally affects the respiratory tract, more often the larynx and bronchi. When the lungs are involved, the amyloid deposition may be diffuse or localized. Focal deposits may simulate neoplasm.

Metastatic Calcification of the Lungs. This condition refers to a metabolic disorder in which lime salts are deposited in presumably previously healthy tissues. Metabolic calcification of the lungs may occur in the presence of chronic renal disease in association with hyperparathyroidism, destructive bone lesions, pro-

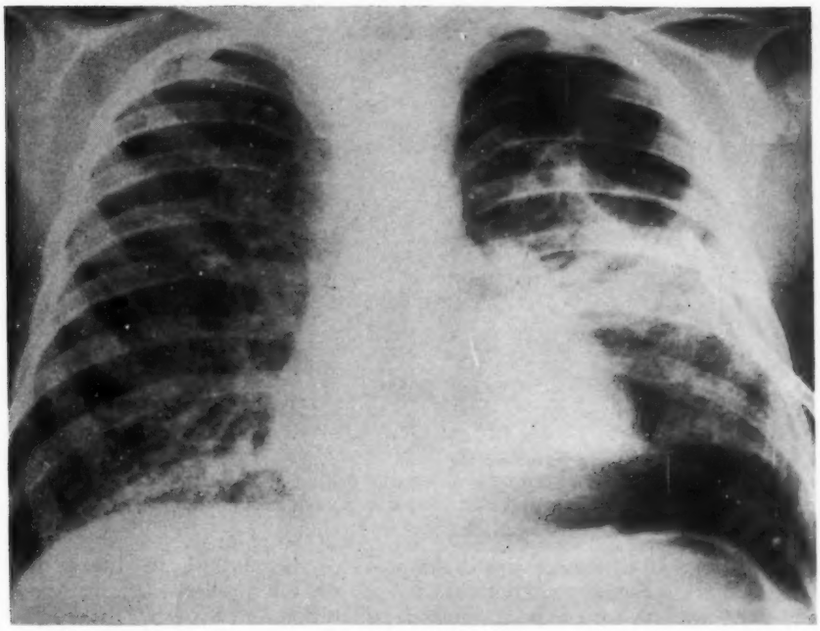

FIG. 2. Histiocytosis with pulmonary involvement. Chest x-ray showing diffuse, lace-like reticulations with minute cysts throughout right lung; similar changes in left lung obscured by a pneumothorax (spontaneous); catheter in situ. (History of purpuric skin eruption; jaundice; generalized lymphadenopathy; enlarged liver and spleen; autopsy showed cystic lungs with numerous blebs on surface; yellowish foci scattered in parenchyma; histologic picture in keeping with Letterer-Siewe disease.)

longed use of highly potent vitamin D preparations or excessive intake of milk and absorbable alkali. The changes in the lungs are rarely recognized during life excepting in cases of calcifying malignant neoplasms with pulmonary metastases.

DISEASES OF THE BLOOD

Diseases of the blood and blood-forming organs seldom affect the lungs. Of particular interest is the occasional encounter of bizarre blood findings in association with intrathoracic conditions. Acute hematogenous tuberculosis may be associated with a myeloblastic blood picture; more often with a relative or absolute leukopenia. In the presence of massive splenic involvement, there may be an associated polycythemia, the condition simulating Banti's disease. Malignant intrathoracic neoplasms may also be associated with leukemoid blood findings; on rare occasion, with eosinophilia or hemolytic anemia. Cavernous hemangioma of the lung, if it causes anoxia, is associated with a compensatory polycythemia in addition to other evidence of oxygen-lack such as dyspnea, cyanosis and digital-clubbing.

Sickle Cell Anemia. The pulmonary manifestations of this blood dyscrasia, affecting Negroes almost exclusively, have received little study although respiratory tract infections are common, frequently precipitating crises and causing death. The changes in the lungs, as in other organs, are characterized by capillary stasis, a tendency to thrombus formation and infarction. The chest x-ray in a patient with sickle cell anemia is seldom "normal." The lungs may show increased bronchovascular striations, patchy infiltrations or evenly dispersed nodular densities. As might be expected, pulmonary tuberculosis is a frequent occurrence. (Fig. 3.)

Pulmonary Hemosiderosis. Endogenous deposits of iron particles in the lungs may be found in association with mitral stenosis or as a result of repeated blood transfusions or after excessive or prolonged parenteral intake of iron, or as an idiopathic disturbance associated with hemolytic anemia. The lungs reveal fine infiltrations which bear a superficial resemblance to miliary tuberculosis; in the idiopathic form there is a veil-like shadow obscuring lung detail. (Fig. 4.)

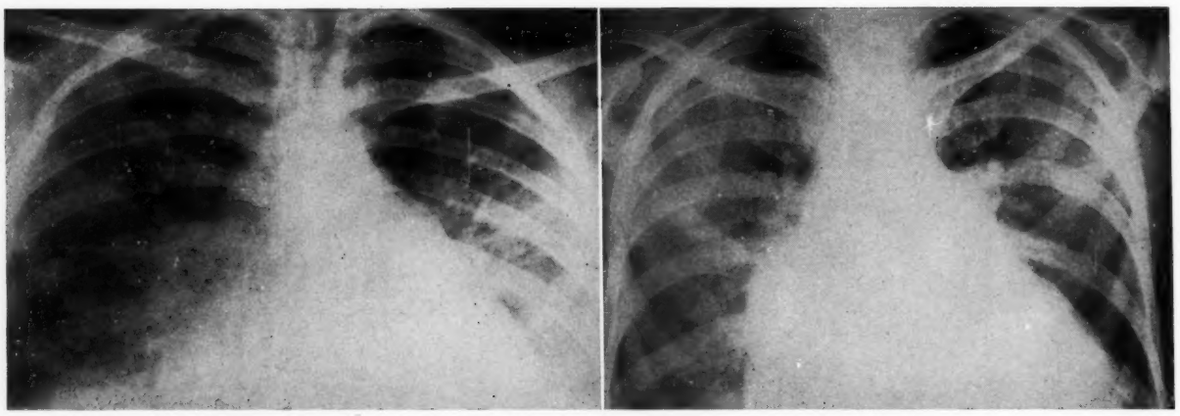

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FIG. 3. Sickle cell anemia with pulmonary manifestations in a Negro woman. Chest x-ray showing patchy and linear infiltrations in both lungs; irregular, triangular density in right mid-lung; heart enlarged; conus prominent. (Admitted late in pregnancy in acute respiratory distress; also generalized edema; delivered stillborn; signs of acute pulmonary congestion abated and patient was discharged improved.)

FIG. 4. Hemosiderosis of lungs in a woman with decompensated rheumatic heart disease. Chest x-ray showing heart greatly enlarged; miliary infiltrations in both lungs especially mid-portions. (Patient died; autopsy revealed old rheumatic mitral valve with stenosis and insufficiency; dilatation and hypertrophy of left auricle, right ventricle and right auricle; chronic passive congestion of lungs, liver and spleen; siderosis of lungs, the parenchyma showing focal deposits of dark-staining iron pigment in perivascular and interstitial tissues.)

Polycythemia. In polycythemia vera one may find an accentuation of the bronchovascular markings, also infiltrations and discrete spherical lesions in the mid-zones of the lungs. In polycythemia associated with pulmonary vascular sclerosis, the middle and peripheral zones of the lungs are within "normal" limits in spite of the unusual prominence of the right heart and pulmonary conus.

Hemorrhagic Diseases. Blood dyscrasias associated with abnormal tendencies to bleeding rarely affect the lungs.

Leukemia. The roentgen manifestations of the leukemias do not differ significantly from those encountered in Hodgkin's disease or lymphosarcoma. The most frequent findings are enlarged hilar lymph nodes with little evidence of extension of the process into the adjoining parenchyma. Isolated leukemic infiltrations are seldom recognized roentgenologically although collections of leukemic cells are often seen microscopically in the tissues. Pleural involvement occasionally accompanies the lymphocytic form of leukemia.

Infectious Mononucleosis. This disease is generally regarded as caused by a specific viral infection although there is little convincing proof to this effect. The hematologic findings are incidental to the systemic manifestations. Pulmonary involvement is quite common, the picture being that of an atypical pneumonia.

DISEASES OF HYPERSENSITIVITY

The introduction of routine chest photofluorography in the examination of general hospital admissions is instrumental in the discovery of increasing numbers of patients with pulmonary manifestations of allergic diseases.

Transitory Pulmonary Infiltrations and Eosinophilia (Loeffler's Syndrome). Fleeting pulmonary infiltrations associated with eosinophilia in allergic subjects represent patches of eosinophilic pneumonia. The condition is also met in association with infestations of parasites, fungi and higher bacteria. The lungs reveal irregular densities of a soft or nodular character appearing in one part of the lung and disappearing in another. This may take a week or longer. Occasionally the chest x-ray reveals massive involvement, upper lobe disease simulating tuberculosis; lower lobe disease, atypical pneumonia. *Loeffler's syndrome* should be distinguished from *tropical eosinophilia.* The latter is featured by a prolonged course, the presence of an enlarged spleen, a high incidence of positive serologic tests for syphilis, positive cold agglutinins, the frequent demonstration of mites in sputa or stools and usually a ready response to arsenic treatment. (Fig. 5.)

Severe and Protracted Forms of Pulmonary Infiltrations and Eosinophilia. The patients

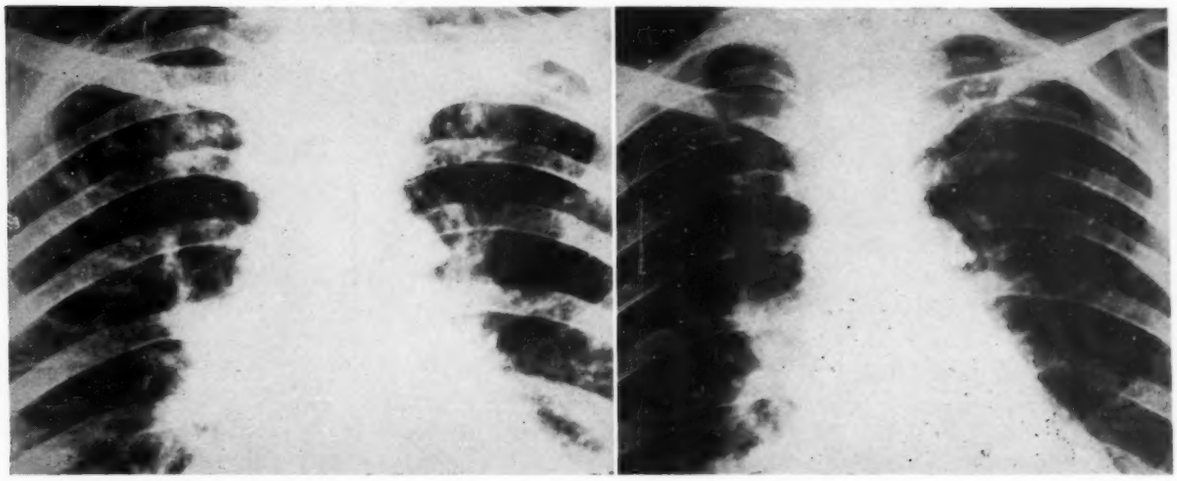

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FIG. 5. Transitory pulmonary infiltrations with eosinophilia in an asthmatic woman. A, chest x-ray showing irregular, soft densities in both lungs. B, one month later clearance of infiltrations, calcific foci in left apex and left hilar region, remains of a healed primary tuberculosis. (Differential diagnosis of active pulmonary tuberculosis and Loeffler's syndrome; sputum negative for acid-fast organisms; eosinophilia 19 per cent; rapid resolution of infiltrations.)

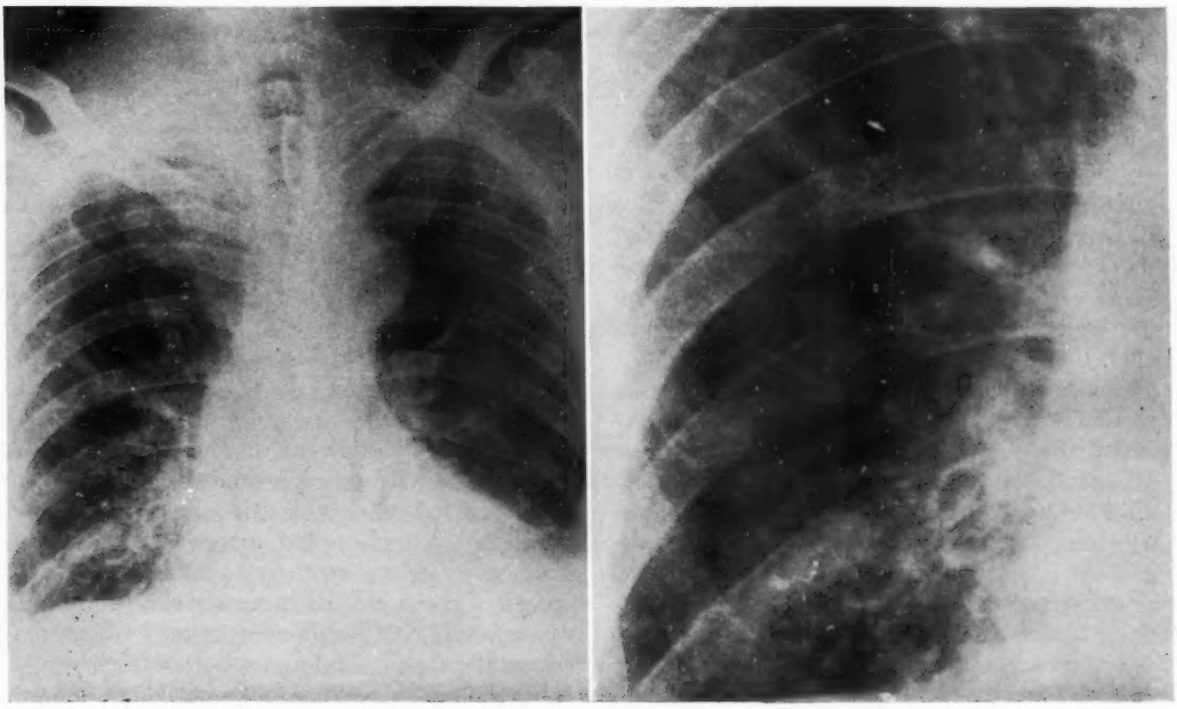

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FIG. 6. Polyarteritis nodosa in an asthmatic man with pulmonary involvement. A, chest x-ray showing nodular and reticular infiltrations in both lungs, especially right; pleuritis, left base; enlarged heart. B, right lower lobe showing detail. (Eosinophilia 22 per cent; hypertension; prostate previously removed because of dysuria showed polyarteritis and eosinophilic granuloma; autopsy revealed arteritic changes involving heart, urogenital organs, muscles and lungs.)

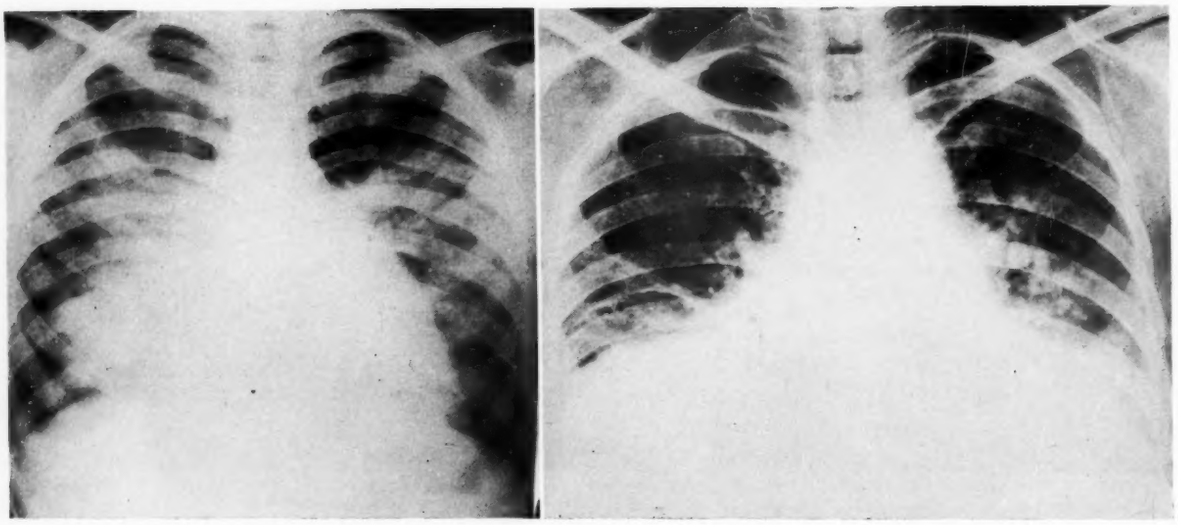

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FIG. 7. Rheumatic pneumonia in a girl of 10 associated with acutely progressive rheumatic heart disease. Chest x-ray showing irregular, fluffy densities extending fanwise into midportions of both lungs; heart enlarged. (Two weeks previously the heart was only slightly enlarged and the lungs clear; total duration of illness 7 months; patient died; autopsy showed rheumatic endocarditis of mitral and tricuspid valves; congestion and edema of lungs with thickening of interlobular septa and mononuclear cell permeation in keeping with rheumatic pneumonia.)

FIG. 8. Rheumatoid disease with pulmonary manifestations in a woman. Chest x-ray showing diffuse interstitial striations in both lungs; prominence and upward displacement of horizontal fissure on right; pleural reaction at bases; heart enlarged. (Allergic background; joint pains paralleled paroxysmal seizures of dyspnea; symptomatic improvement with cortisone.)

are more acutely ill and for longer periods. The pulmonary involvement is more extensive and often associated with complicating pleural and pericardial effusions. There may be coexisting hyperergic reactions in other organs with evidence of generalized vasculitis.

Polyarteritis Nodosa. The changes in the lungs partake of the same features characterizing the disease in other organs. The most frequent findings histologically are whitish nodules along blood vessels, chiefly the pulmonary and bronchial arterioles, also granulomatous lesions, infarcts and even cavitation. The chest x-ray findings, although not characteristic of the disease, may be in keeping with it. The changes consist of accentuated vascular and perivascular markings, a nodularity in the mid and inner portions of the lungs or diffuse uneven densities often associated with pleuritis and pericarditis. (Fig. 6.)

Rheumatic Pneumonia. This condition occurs in a small number of patients with rheumatic fever. The clinical and roentgen features of rheumatic pneumonia are not sufficiently distinctive to enable one to differentiate it from pulmonary congestion and infarction. But in the absence of signs of heart failure, the appearance of miliary or patchy infiltrations in both lungs, particularly in the upper and mid zones, occurring early in the development of the rheumatic state is suggestive of the lung disease being part of the rheumatic state. (Fig. 7.)

Rheumatoid Disease with Pulmonary Lesions. Rheumatoid disease is a more descriptive term than rheumatoid arthritis since the former expresses a widespread disturbance involving not only the locomotor system but also other parts of the body. Rheumatoid disease may be associated with pulmonary lesions which may simulate atypical pneumonia, acute rheumatic pneumonia or diffuse interstitial pulmonary fibrosis. In some cases these several manifestations represent one and the same disease. Rheumatoid disease is a member of a group of disorders including polyarteritis nodosa, rheumatic fever, scleroderma, dermatomyositis and several others which are sometimes referred to as "collagen diseases." The changes involve chiefly the connective tissues of the body.

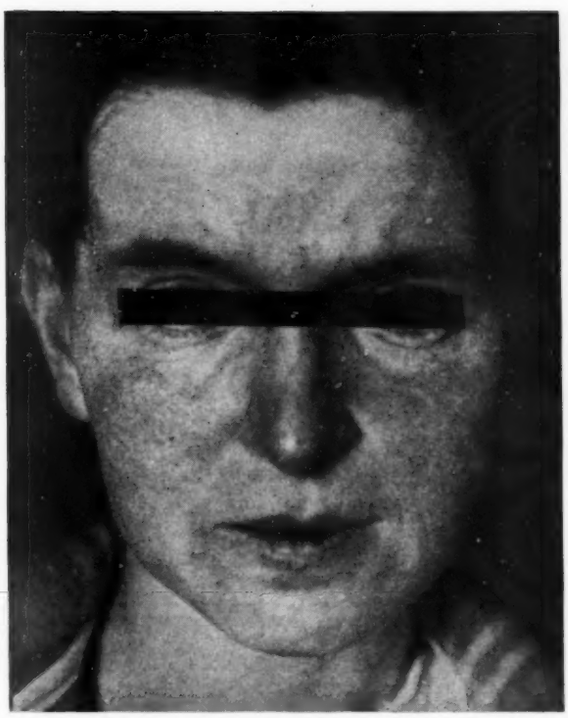

FIG. 9A. Systemic lupus erythematosus with pleuropulmonary and pericardial manifestations in a young woman. Characteristic butterfly rash on bridge of nose and cheeks.

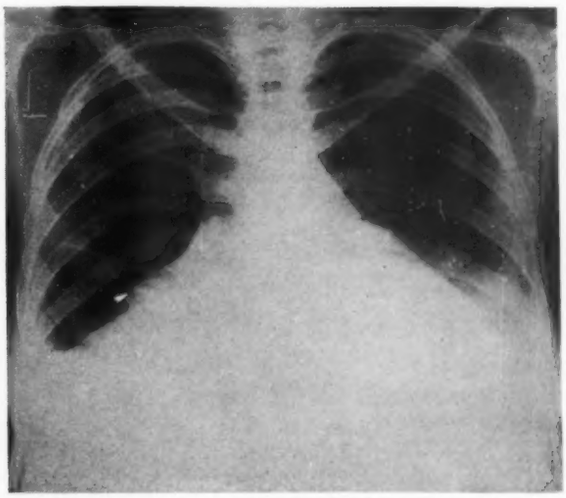

FIG. 9B. Same case as Figure 9A. Chest x-ray showing signs of fluid in pleural cavities and pericardium; soft, round infiltration in right upper lobe; linear, horizontal striations in right mid-lung. (Five months previously chest x-ray showed no abnormalities; rapidly progressive course with fatal issue; autopsy revealed fibrinous, gelatinous exudate in pleural cavities; also in pericardial sac; edema and congestion of lungs; glomerular lesions in kidneys with suggestive "wire-loop" appearance.)

Quite often the several conditions mentioned overlap. (Fig. 8.)

DISEASES OF THE SKIN AND MUCOUS MEMBRANES

In the usual type of skin disease encountered in practice a chest x-ray is seldom considered necessary and as a result much important information which might be obtained by this means does not come to light. Yet there is ample evidence that even in apparently superficial skin diseases other organs including the lungs may be implicated. Discerning dermatologists have for years stressed the fact that few skin diseases are "skin deep."

Allergic Dermatitis. Transitory pulmonary infiltrations with eosinophilia may punctuate the course of acute and chronic neurodermatitis and other atopic skin diseases. The clinical and roentgen findings are similar to those encountered in Loeffler's syndrome. Pulmonary infiltrations with eosinophilia may also be encountered in patients sensitive to penicillin, mercury compounds, barbiturates as well as in association with skin eruptions caused by cutaneous helminthiasis.

Erythema Multiform. This disease is characterized by pleomorphic changes in the skin, chiefly of the extensor surfaces of the limbs, consisting of erythema, papules and/or vesicles and bullae. Some investigators believe that the disease, at least in some patients, is caused by hypersensitivity to drugs or bacterial or viral products. The pulmonary manifestations may take the form of a simple bronchitis in association with acute mucosal lesions of the mouth, larynx and pharynx which feature the disease. If the lungs are involved, the chest x-ray may reveal nodular densities, scattered patchy infiltrations or massive consolidations.

Erythema Nodosum. The lesions in this disease are characterized by discrete, red, tender nodules of varying size which appear in crops in the subcutaneous tissues especially of the forearms and legs. The intrathoracic manifestations concern chiefly, often exclusively, the hilar lymph nodes. But the lung parenchyma may be involved without noteworthy participation of the lymph nodes. The roentgen findings bear a striking resemblance to those met in sarcoidosis to be described shortly; in fact, some investigators consider

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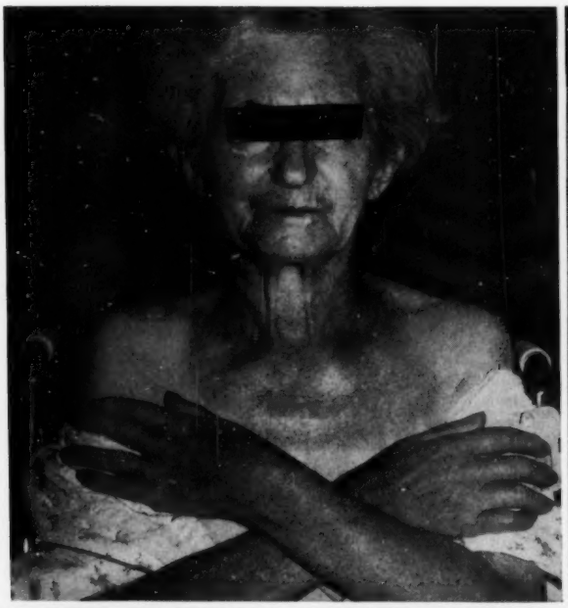

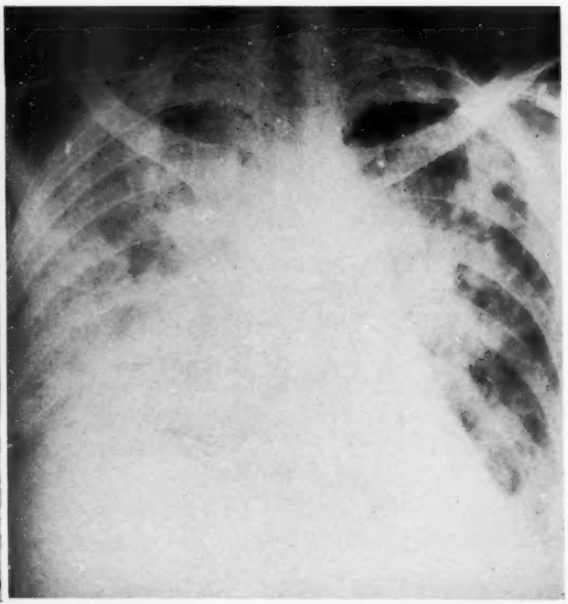

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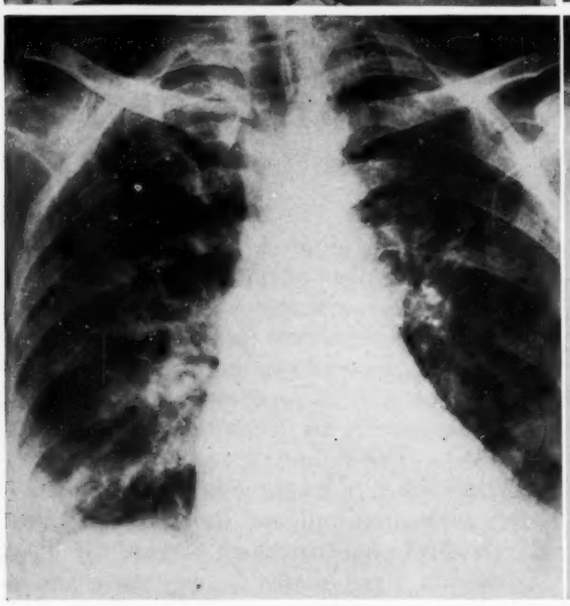

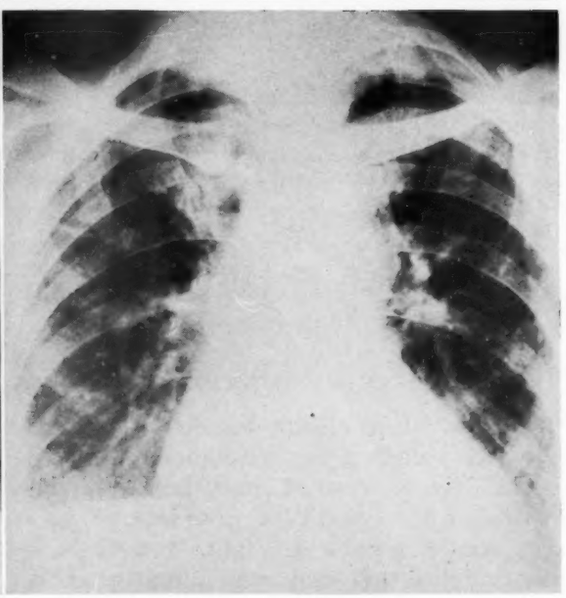

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FIG. 10. Scleroderma, lupus erythematosus and rheumatoid disease in a woman. A, photograph showing characteristic facies of scleroderma; puckered lips; also (erythematous) rash over the V of the neck; (rheumatoid arthritis; Raynaud's phenomenon; L. E. positive; pleural and pericardial friction rubs). B, bedside chest x-ray at onset of illness showing massive infiltrations involving both lungs with pleuritis (clinical course of acute, non-bacterial pneumonia). C, Three weeks later considerable resolution of pneumonic process leaving diffuse interstitial striations and patchy consolidations; heart moderately enlarged. D, six months later increasing organization of diffuse interstitial fibrosis of both lungs. (Courtesy Dr. Sol Biloon.)

both manifestations of the same morbid state.

Systemic Lupus Erythematosus. This disease, affecting chiefly females, is characterized in its classic form by a butterfly erythema on the bridge of the nose and cheeks, the skin being sensitive to light, drugs and irritants of any type. Older lesions show atrophy, telangiectasis and pigmentation. Since the introduction of the L.E. cell test, aberrant forms are often encountered. It has been known for sometime that the disease may involve various organs and not implicate the skin. The pleuropulmo-

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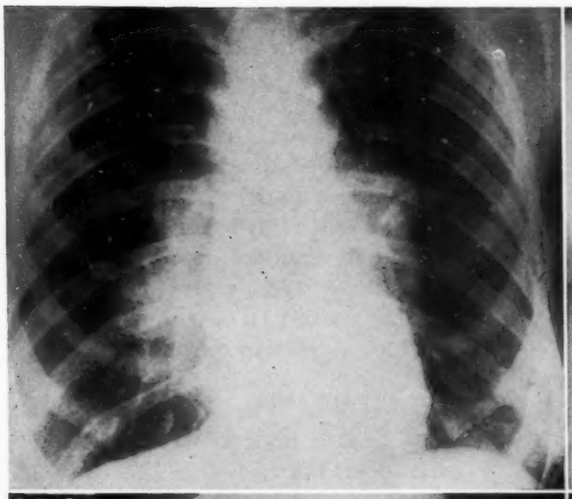

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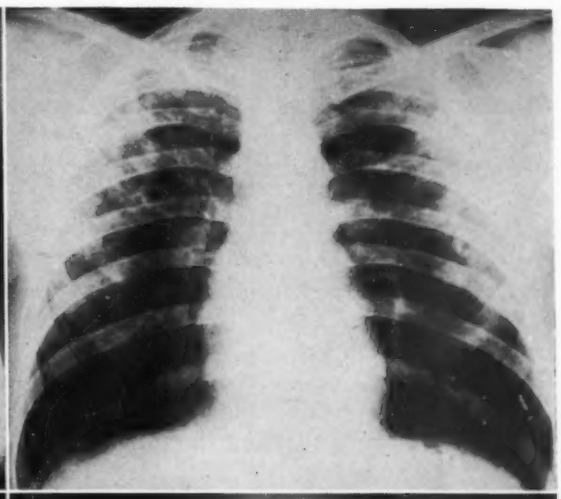

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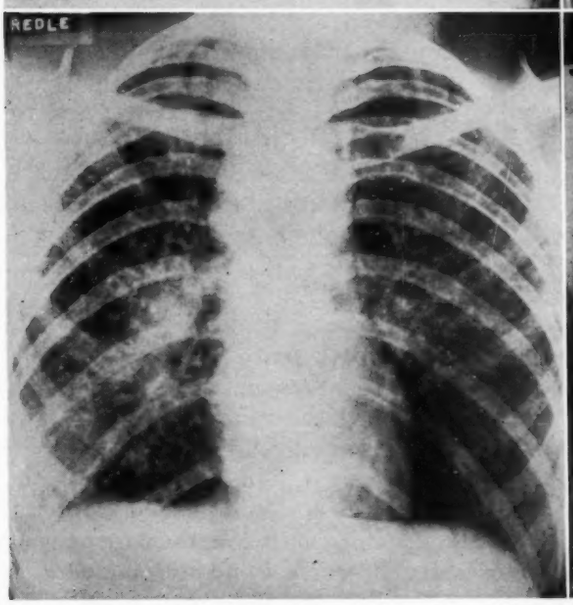

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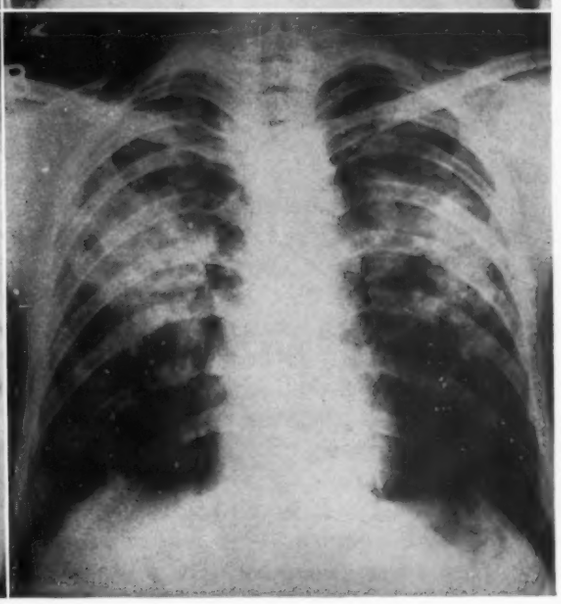


FIG. 11. Sarcoidosis: diagnosis confirmed histologically. A, chest x-ray showing enlarged hilar and paratracheal lymph nodes in a woman with clinical signs of uveoparotid fever (Heerfordt's disease) simulating Hodgkin's disease. B, chest x-ray showing diffuse reticular striations of upper lobes and emphysema of lower lobes. (Five years later, advanced emphysema.) C, Chest x-ray showing enlarged right hilar and paratracheal lymph nodes; also nodular infiltrations throughout both lungs simulating miliary tuberculosis. (Patient went through pregnancy successfully, sarcoidosis resolved spontaneously.) D, chest x-ray showing dense masses of irregular infiltrations in both upper lobes; apices and lower lobes hyperilluminated, simulating fibroid tuberculosis for which patient was sent to a sanatorium. (In the course of nine years increasing fibrosis of upper lobes and emphysema of lower lobes; chronic cor pulmonale; no evidence of tuberculosis; autopsy confirmation.)

nary manifestations have received little attention possibly because the lungs do not show as striking features of the disease as do the heart, kidneys, joints and hemopoietic organs. Yet there is hardly a patient with acute systemic lupus erythematosus who does not show pulmonary involvement, especially of the pleura, at some time during the course of the disease. Occasionally the pulmonary lesions may precede other localizations. (Fig. 9.)

Mycosis Fungoides. This disease, closely related to malignant lymphomas, is characterized by erythematous, eczematoid, urticarial or mixed lesions of the skin which infiltrate and thicken the epidermis producing in time nodular, ulcerating or fungating masses.

X-ray of the chest may reveal prominent hilar markings and round infiltrates in the lung parenchyma.

Neurocutaneous Diseases. Of late, internists are becoming increasingly interested in a number of syndromes hitherto in the domain of neurologists because the conditions may be associated with systemic lesions. In tuberous sclerosis one may find innumerable large and small cysts in both lungs producing a "honeycomb" appearance. In von Recklinghausen's disease (neurofibromatosis) the chest x-ray may reveal intrathoracic neurofibromas in association with the intercostal, vagus and sympathetic nerves. On rare occasion the lung parenchyma may be involved.

Scleroderma. This disease is featured by hardening of the skin and mucous membranes, the result of an initially diffuse, non-pitting edema of the connective tissue. After edema subsides, the stroma is replaced by fibrous tissue leading to atrophy of the skin and underlying structures. An accompanying vascular disturbance may give rise to Raynaud's disease. The pulmonary changes consist of a widespread interstitial fibrosis or cystic sclerosis of the parenchyma, the latter probably representing a later stage of the former. There is some evidence that malignant neoplasms of various organs, including the lungs, occur with considerable frequency in association with scleroderma. (Fig. 10.)

Dermatomyositis. This condition is characterized by the insidious development of fatigue, muscle pain and weakness. The cutaneous changes consist of puffiness of the face and an erythematous rash of the neck, ears, chest and shoulders, also of the dorsum of the hands. Abnormal changes in the lungs are not a feature of the disease. However, increasing numbers of cases are being reported of dermatomyositis associated with malignant neoplasms, a combination which appears to be more than a coincidence.

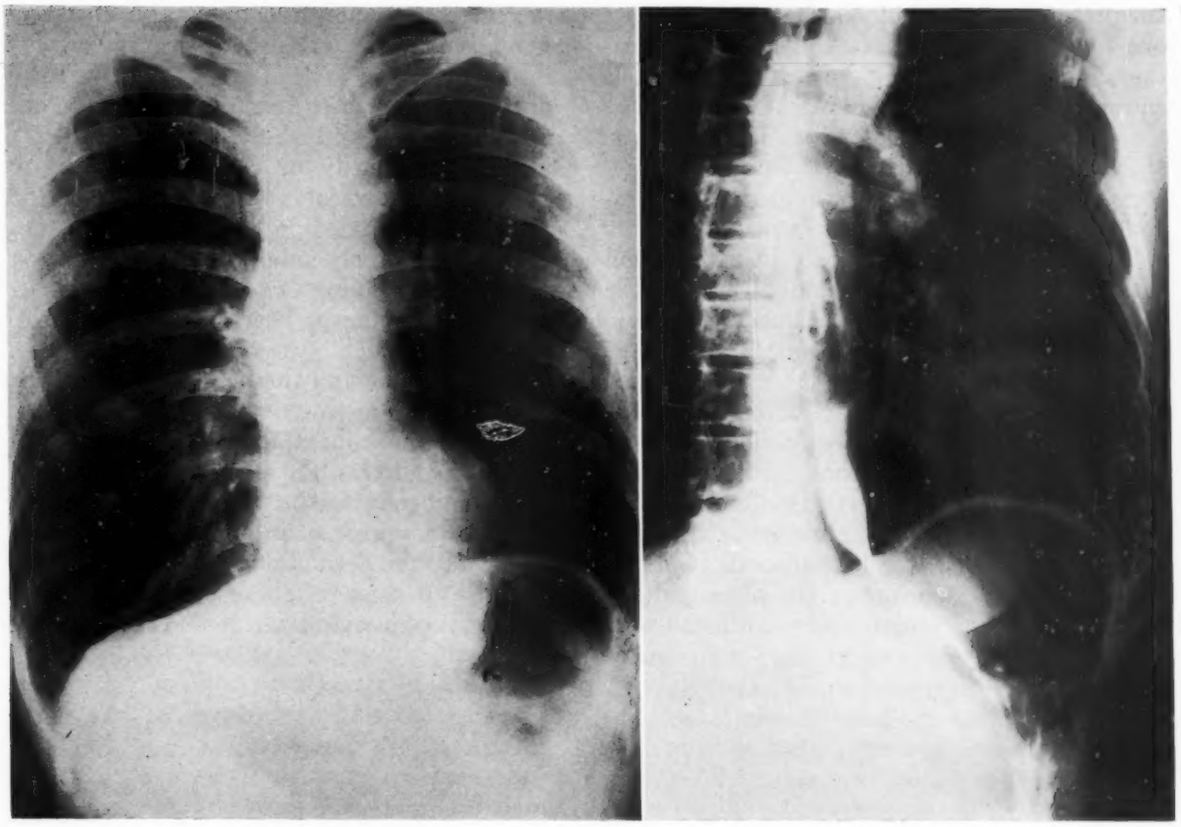
Acanthosis Nigricans. This striking skin disease is characterized by the development of darkly pigmented, furrowed ridges on the exposed surfaces of the body, especially of the folds of the skin. A benign form occurs in young people; a malignant form, in later life. For some unexplainable reason the latter is often associated with cancer of viscera, especially of the stomach, also of the lungs.

Sarcoidosis. Originally described by Boeck as a skin disease, sarcoidosis is now recognized as a systemic disorder often involving intrathoracic structures. The disease is characterized by disseminated nodules in organs and tissues, histologically showing tubercle-like structures composed of epithelioid cells, small numbers of lymphocytes and giant cells of the Langhans type. Intrathoracic sarcoidosis is often discovered accidentally in the course of routine chest roentgenography. Three broad roentgenologic patterns of the disease in the chest which often overlap may be distinguished: (1) a hilar form, (2) a transitional form and (3) a parenchymal form. The hilar form is featured by massive lymph node enlargement. At this stage, sarcoidosis may be mistaken for a malignant lymphoma. The transitional form is featured by hilar lymph node enlargement and reticular striations throughout both lungs simulating lymphangitic carcinoma. The parenchymal form may assume miliary, nodular, fibro-emphysematous and other patterns. These simulate pulmonary tuberculosis, fungus infections and dust inhalational diseases. (Fig. 11.)

PLEUROPULMONARY MANIFESTATIONS OF ABDOMINAL DISEASES

In the limited space available it will be possible to mention only a few abdominal conditions which may show roentgenologically signs of their presence in the chest.

Surgical Diseases. In the course of routine chest x-rays of newly admitted patients to general hospitals with "acute surgical conditions of the abdomen," one finds occasionally a collection of free air under one or both leaves of the diaphragm. The discovery of a pneumoperitoneum indicates the presence of a perforated abdominal viscus. At other times one may note the diaphragm to be abnormally elevated by gaseous distention of the bowel, the latter possibly showing fluid levels in keeping with strangulation of the gut. A shadow caused by a tumor may be visible in the air-filled segment of the stomach. (Fig. 12.) A rounded density at the right cardiodiaphragmatic angle may indicate the presence of a parasternal hernia. The chest x-ray is of inestimable value in the detection of pleuropulmonary complications following abdominal operations. The incidence of atelectasis, pneumonia and pleural effusion is notoriously high after operations on the stomach, duodenum and biliary tract. In such cases there is a paucity of clinical evidence



12A 12B

FIG. 12. Carcinoma of stomach discovered accidentally in routine chest x-ray. A, chest x-ray showing rounded edge of a density at cardia of stomach. B, mass seen more clearly after barium meal. (At operation a carcinoma was found originating at lower end of esophagus and protruding into stomach; subtotal gastrectomy and gastro-esophagostomy done.)

of pleuropulmonary involvement and the patient may be allowed to leave the hospital with a smoldering focus in the chest.

Chest Findings in the Presence of Other Abdominal Diseases. The chest x-ray is instrumental in the discovery of displacements and intrinsic disease of the diaphragm as well as in localizing collections of fluid above or immediately below the muscle. A discussion of these and related subjects is beyond the scope of this review. However, there are two types of roentgen abnormalities which may be associated with intra-abdominal disease deserving of comment. These are the occurrence of linear, horizontal striations, and/or unexplained pleural effusions the recognition of which may be helpful in the diagnosis of obscure abdominal disease.

Linear densities running transversely across one or both lower lung fields may be present in association with intrathoracic as well as abdominal disease, more often with the latter. Fleischner was among the first to draw attention to the significance of these linear striations which represent atelectatic lung. The atelectatic area is discoid in shape lying in more than one plane of the lung. They appear in the chest x-ray either as single or multiple horizontal densities in one or both lower lung fields, at times in association with pleural effusion. The abdominal conditions which may be found in association with pulmonary atelectasis of the type described are many and diverse including inflammatory lesions (liver abscess, subdiaphragmatic abscess, acute and subacute pancreatitis) and neoplasms (tumors of the ovary, gallbladder and gastrointestinal tract).

The conditions listed which may cause pulmonary atelectasis may also provoke pleural effusion. In most instances the effusion is due to direct extension of the inflammatory or neoplastic process to the diaphragmatic pleura. In

the presence of acute subdiaphragmatic disease one may also encounter a transient, "sympathetic" effusion; usually, however, the fluid is caused by infection. Of particular interest is the finding of a large collection of fluid in the chest, usually a right-sided hydrothorax, accompanied by ascites in the presence of intra-abdominal tumors, notably ovarian tumors (Meigs' syndrome) but also in association with cirrhosis of the liver and several of the other conditions already mentioned.

CONCLUDING REMARKS

This review deals briefly with the intrathoracic manifestations of a number of systemic diseases, including those of metabolism, blood, skin and neurocutaneous structures, those of probable allergic origin and of several abdominal conditions. The limited space available does not permit inclusion of the pleuropulmonary changes accompanying cardiovascular diseases, systemic infections and metastatic neoplasms. The purpose of the review is to draw attention to the wealth of information often available in the examination of the chest x-ray, not only in the diagnosis of diseases affecting primarily or chiefly the lungs and pleura, but also of generalized disturbances commonly included in the field of "internal medicine" and its subdivisions (dermatology, allergy, metabolism, endocrinology, hematology and neurology). There are times when the presence of such systemic diseases may be detected earlier and their nature better appreciated in their mirrored appearance in the lungs than in more vulnerable organs which are not as readily accessible to inspection. To the opthalmologist the interior of the eye often serves as a mirror of internal disease, so does the skin to the dermatologist and, as I have attempted to show in these pages, this applies also to the physician interested in chest diseases.

Pulmonary Roentgenologic Changes in the Collagen Diseases

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THE respiratory and cardiovascular systems are commonly involved in the so-called collagen diseases. This article will outline the more conspicuous pleuropulmonary changes and the associated pericardiovascular changes which are encountered in this group of disorders.

The collagen diseases are a group of disorders characterized anatomically by generalized alterations of the connective tissue, especially of its extracellular components. The currently accepted members of this group are periarteritis nodosa, disseminated lupus erythematosus, dermatomyositis, scleroderma, rheumatic fever and rheumatoid arthritis.

The term polyarteritis is synonymous with periarteritis nodosa. Because of the predominance of vascular changes, this disorder (and, to a lesser extent, generalized lupus erythematosus) may also be referred to as visceral angiitis. Disseminated lupus erythematosus is also known as acute lupus erythematosus or generalized lupus erythematosus.

Becker[2] and others believe that the systemic manifestations of Schönlein-Henoch purpura, erythema nodosum and certain cases of glomerulonephritis include similar involvement of connective tissue and may belong to this group of diseases. Ehrich and associates,[8] on the basis of animal experiments, would also include serum sickness. Kampmeier[16] has suggested that the necrotic changes found in afferent renal arteries in both malignant hypertension and periarteritis nodosa have more than coincidental relationship. Stewart[29] believes that thromboangiitis obliterans and ulcerative colitis are also collagen diseases.

ETIOLOGY AND PATHOLOGY

The etiology of the collagen diseases is not known. Several workers have produced fibrinoid changes of connective tissue experimentally by mechanical and by chemical means.[5] These observations tend to invalidate the supposition that hypersensitivity is the sole cause of collagenous degeneration. Indeed, it has been observed that undue significance should not be attached to the occurrence of fibrinoid changes in localized connective tissue collagen. Pathologically, this is merely a form of degeneration, unspecified in etiology, and occurring in a wide variety of dissimilar diseases. This fact, of course, greatly minimizes the clinical usefulness of the term collagen disease. However, until a better term is devised and until we know more about the fundamental nature of the diseases in question, it is probably justifiable to continue the use of the term. In this connection, it is to be noted that the microscopic findings do not consist merely of changes in the collagen fibers alone, but of changes in the connective tissue elements as a whole.

Histologically, connective tissue consists of cellular elements and extracellular substances. The cellular elements consist of fibrocytes and fibroblasts, macrophages, lymphoid cells, mast cells and various other leukocytes. The extracellular substances are composed of an amorphous ground substance and three known types of fibers, namely, collagenous, reticular and elastic. The basic lesion in the collagen diseases consists of a swelling of the interfibrillary ground substance as well as swelling of the fibers themselves. The location of these basic lesions and the type of response of the adjacent tissues are somewhat different in the different collagen diseases, and constitute the anatomic basis by which they may be at least partly distinguished.

Abnormal collagen may be detected by suitable x-ray diffraction studies and electron microscopy. Kellgren believes that this will prove a useful method for diagnosing connective disorders.

Not all clinical subdivisions of the collagen diseases are clearly demarcated. In some patients, at necropsy, lesions peculiar to or predominant in some of the different entities may be found in one and the same patient. For example, a fatal case may show: (1) chronic skin lesions, as in scleroderma; (2) atrophy of skin, and degeneration of muscle, as in dermatomyositis; (3) proliferation of endothelial capillary tissue, as in disseminated lupus erythematosus; (4) non-bacterial verrucous endocarditis;* (5) infiltration and dilatation of arterioles, as in periarteritis nodosa; (6) pericardial changes, as in rheumatic infection; and (7) articular and tenosynovial changes, as in rheumatoid arthritis.

A case embodying all these diverse manifestations was recorded by Kampmeier.[16]

Miale[21] mentions that Krupp first emphasized a characteristic urinary finding in "visceral angiitis"; he found the pattern in fourteen of twenty-one cases of periarteritis nodosa and disseminated lupus erythematosus. It consists of the simultaneous presence of elements usually characteristic of the early stages of nephritis (erythrocytes and erythrocytic casts), and elements usually seen in the chronic stage (broad casts, waxy casts, fatty casts and "oval fat bodies"). This finding has been referred to as a "telescopic urinary sediment."

CLINICAL TYPES AND SOURCE OF MATERIAL

The types of collagen disease to be discussed in the following pages include periarteritis nodosa, generalized lupus erythematosis, dermatomyositis and scleroderma. Space will permit only brief mention of the two more common entities, rheumatic fever and rheumatoid arthritis.

The cases studied were obtained by a review of the files in the roentgen departments and the record rooms at San Francisco Hospital and Stanford University Hospital. The period covered is approximately fifteen years, a majority of the cases having been indexed in the last ten years.

PERIARTERITIS NODOSA (POLYARTERITIS)

Periarteritis nodosa is frequently and more correctly called polyarteritis as there is actually a widespread poly- rather than periarteritis, affecting chiefly the medium-sized and smaller arteries of the body. Pathologically there is a degeneration of the collagenous tissue in the walls of the vessels, sometimes with necrosis of the media, rupture of the elastic lamina and infiltration of inflammatory cells and eosinophils into all of the vascular layers. When this infiltration of the arterial coats is localized, or is followed by local fibrosis, or the development of small aneurysmal dilatations, nodular changes develop (giving rise to the term nodosa).

Clinically the signs and symptoms are determined more by the distribution of the involved arteries than by the disease process itself. Almost any clinical condition may be mimicked. However, a polysystemic involvement with chronic fever, leukocytosis, eosinophilia and secondary anemia suggests the condition, and is an indication for skin and muscle biopsy. Recurrent hemoptysis has been reported by one group (Edwards et al.[7]).

Roentgenologically findings may or may not be present, depending on which systems happen to be involved, and also on the acuteness and degree of that involvement. Cardiac enlargement and/or pericardial effusion occurs. The respiratory system may show massive symmetric or non-symmetric edema in severe acute cases. In others, small hazy shadows or non-confluent patches of edema (pulmonary hives) may be scattered throughout the lung fields, usually peripherally and at the bases.[1] Some authors[9,25] report cases in which the nodulation is most marked centrally. In addition to the nodular densities, the pulmonary linear markings may be accentuated, particularly the hilar and basal ones. Doub et al.[6] report hilar enlargement as a conspicuous finding in a series of ten microscopically proven cases. Pleural effusion, secondary to pneumonitis or pulmonary infarction, is reportedly not uncommon.

Roentgen examination of the abdomen is frequently requested since abdominal pain is one of the most common early symptoms. A triad of myositis, abdominal pain and weight loss has been referred to by some. The abdominal films usually show either no abnormality, or some gas collections suggesting paralytic obstruction (so-called adynamic ileus). Very rarely, there may be a perforated ulcer, intestinal infarction or pancreatic necrosis. One of our cases had both intraperitoneal and retro-

* Non-bacterial verrucous endocarditis, as in Libman-Sacks syndrome, is now known to be part of the changes occurring in disseminated lupus erythematosus.

peritoneal bleeding due to ruptured aneurysm of a small mesenteric vessel, secondary to "healed" arteritis. A hypertension of 200/140 was present; this patient also had multiple duodenal ulcers.

TABLE 1

CHEST ROENTGEN FINDINGS IN THIRTY-ONE CASES OF PERIARTERITIS

No evidence of disease		9
Evidence of disease		22
Cardiac enlargement	6	
Pericardial effusion	6	
Pleural effusion	7	
Pulmonary changes	16	
Parenchymal nodules, patches, etc.	6	
Pulmonary congestion, passive	6	
Accentuated markings, ? arteritis	4	
Pulmonary edema, massive	4	

Note: Some of the cases with "cardiac" enlargement may also have had some pericardial effusion.

Renal lesions are the most common of all the systemic lesions, being present in 80 per cent of the cases.[19] Occasionally hypertension or hematuria may be so prominent that intravenous urograms are requested. These usually show either normal or decreased function.

The records of thirty-two cases of periarteritis nodosa were reviewed. In thirty-one of these, chest films were available and disclosed the findings shown in Table 1. It is to be noted that some cases had more than one finding (e.g., pericardial, pleural and pulmonary lesions).

At autopsy one of our patients had both polyarteritis and rheumatic heart disease (mitral and aortic stenosis with insufficiency). His roentgenograms showed an enlarged heart, pulmonary congestion and pleural effusion.

None of the foregoing roentgen findings are diagnostic *per se* of periarteritis nodosa, but the presence of pulmonary, pleural or cardiopericardial changes in a patient with involvement of other systems, should cause one to bear the possibility of a collagen disease in mind.

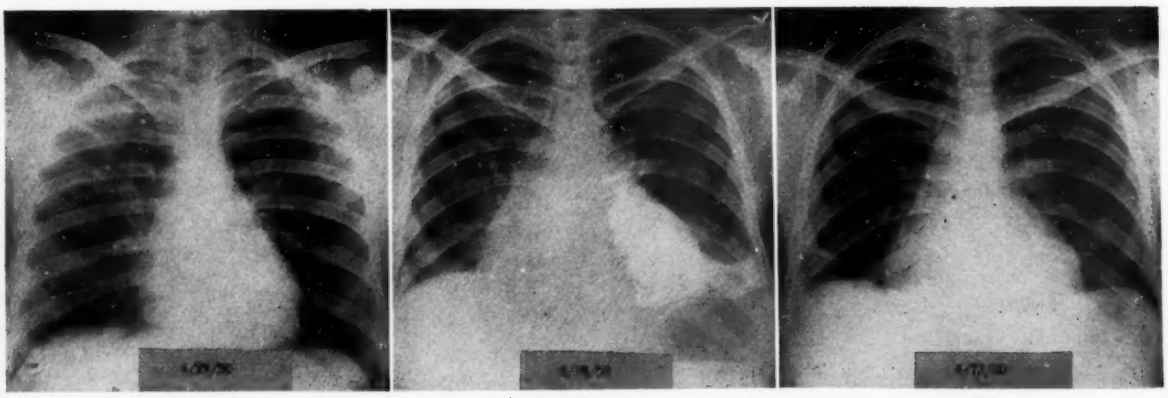
In the entire thirty-two cases adequate roentgenologic records of systems other than the cardiorespiratory were limited. In two cases hepatomegaly and in two cases splenomegaly were noted by our department. One case showed roentgen evidence of mild paralytic ileus. Three cases showed peptic ulcer (one gastric and two duodenal). No cases of gross renal enlargement were recorded, but one did show poor function by excretory urography. No bone changes were noted; three patients showed roentgen evidence of articular disease (two synovial thickening, one rheumatoid arthritis). Biopsy or necropsy material compatible with the diagnosis of periarteritis nodosa was available in twenty of the thirty-two cases. In seven cases biopsy reports were negative, but the clinical evidence was outstanding; two of these patients died apparently of the disease.*

The following are some illustrative cases:

Case E. M. (Fig. 1), a white female, aged twenty-six, had migratory joint pains, low-grade fever, myalgia and patchy gangrene of some of the fingers and toes. She was known to have had periarteritis nodosa for two years. On April 29, 1950, a roentgenographic examination of the chest was negative. Re-examination in two and one-half weeks showed small bilateral pleural effusions and a pericardial effusion. One month later, after cortisone therapy, clinical and roentgenographic improvement was present. This case showed acute development of pleural and pericardial lesions during the course of a chronic multiple system disease. Biopsy of skin and muscle positive for periarteritis nodosa.

Case R. S. (Fig. 2) a sixty-three year old man, had fainting spells of unknown origin for a few weeks, and pain and stiffness of the shoulders and knees since a fall one month prior to entry. Initial chest roentgenograms showed only slight left ventricular enlargement. Two days later, films showed bilateral pleural effusion and pulmonary congestion. Clinically he had become acutely ill, with high fever (up to 103.1°F.), but without evidence of cardiac failure. Roentgen examination four weeks later showed clearing of the congestion and effusions, despite the fact that the patient was failing generally. The urine then showed abnormal findings, the so-called telescopic sediment, and the possibility of "visceral angiitis" became entertained. He recovered

* Most of the histopathologic studies referred to in connection with the cases reported in this paper were made by members of the Stanford University Medical School Department of Pathology staff; in a few instances material was reported by the University of California staff at the San Francisco Hospital, to whom we are indebted.



1A 1B 1C

FIG. 1. Case E. M. Periarteritis nodosa. Development of acute pericardial and bilateral pleural effusions during a chronic illness of two years. Biopsy positive. White, female, aged twenty-six, with arthralgia, myalgia, fever and gangrene of tips of fingers and toes. A, chest film negative; pericardial friction rub present. B, pericardial and bilateral pleural effusions. C, improvement; also improved clinically, under cortisone therapy. (Courtesy of *Am. J. Roentgenol.*)

2A 2B 2C

FIG. 2. Case R. S. Periarteritis nodosa. Rapid development of pericardial and bilateral pleural effusions. Negro, male, aged sixty-three, with fainting spells, fever, pain and stiffness of shoulders and knees. A, lungs clear; questionable left ventricular enlargement. B, pulmonary congestion, pericardial and pleural effusions; patient now acutely ill. C, improved. (Courtesy of *Am. J. Roentgenol.*)

partially and was discharged. Biopsy of skin and muscle was reported negative.

Case L. E. L. (Fig. 3), a white female, aged thirty-four, had asthma for one year and numbness of the left leg and pain in the left foot for six months. She was found to have splenomegaly, eosinophilia and a renal lesion, with casts and cells. Chest films showed pulmonary nodulation, fibrosis and emphysema. Biopsy of skin and muscle was negative. Marked clinical and roentgenologic improvement occurred within three days after cortisone was started. She was discharged improved.

Case R. C. (Fig. 4), a white longshoreman aged forty-five, entered on August 12, 1948, with chills, fever (101°F.), mild cough, chest pain and dyspnea. He had had a dermatitis of his leg for two years, with local ulceration. Pain in the right upper abdominal quadrant, a markedly enlarged liver and massive hematuria were present. He had a hypertension of 180/80; his blood urea was 27 mg. per cent; the white blood cell count was normal. Roentgenograms showed clouding of the right upper lobe and of the left mid-lung field, interpreted as pulmonary edema; moderate splenomegaly was noted on abdominal film. Nine days after entry the patient was clinically and roentgenologically improved. Biopsy was not performed. A year later his chest film continued to be negative.

Case G. H. B., a white male, aged forty, was clinically diagnosed as having rheumatoid arthritis. Roentgenograms showed cardiomeg-

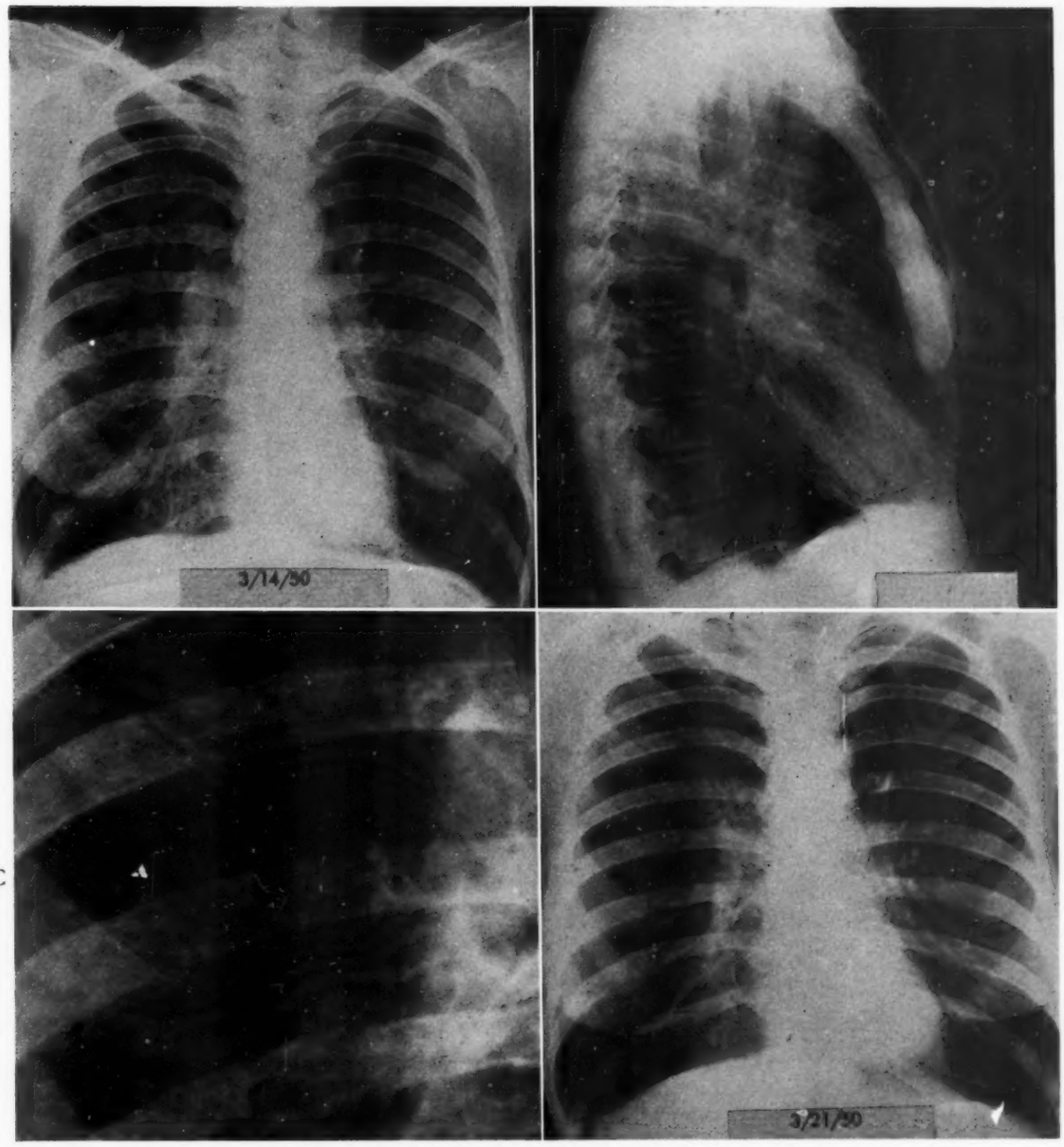
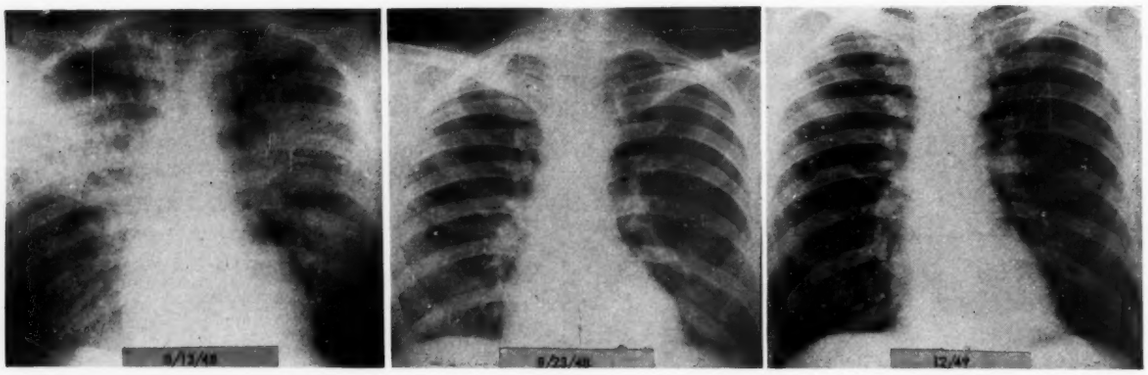


FIG. 3. Case L. E. L. Periarteritis nodosa. Pulmonary nodulation and improvement under cortisone therapy. White, female, aged thirty-four. Asthma for one year; then leg pains, eosinophilia, splenomegaly, and renal lesion with casts and cells. A, pulmonary nodulation and possible emphysema. B, lateral view. C, close-up of right mid-lung field. D, marked improvement on fourth day of cortisone therapy.

aly, predominantly left ventricular, and bilateral pleural effusion. The patient died shortly after examination, apparently from cardiac failure. Autopsy showed: (1) diffuse collagen disease with polyserositis (peritoneal, pleural and pericardial fluid); rheumatic heart disease (aortic valve stenosis); "wire-looping" of renal glomeruli (as in lupus erythematosus); rheumatoid arthritis; periarteritis nodosa (of pulmonary, thyroid and testicular arteries). (2) Pulmonary emphysema (and fibrosis). (3) Generalized arteriosclerosis (coronary, aortic and renal).

This case illustrated a combination of four types of "collagen" disease—periarteritis nodosa, lupus erythematosus, rheumatoid arthritis and rheumatic carditis.

Case I. S. (Fig. 5), a female singer, age thirty-one, was hospitalized for mental disturbance. She stated that she had had severe asthma for



4A 4B 4C

FIG. 4. Case R. C. Acute periarteritis nodosa, with asymmetric pulmonary "edema." White, male, longshoreman, aged forty-five. Four days previously onset of chilliness, fever (101°F.), mild non-productive cough; then right upper quadrant pain, massive hematuria, some hepatomegaly. Eosinophilia 9 per cent, blood urea 27 mg. per cent. A, on fourth day of illness showing densities suggesting pulmonary edema. B, improved, roentgenologically and clinically. C, one year later, chest negative.

sixteen months with muscle and joint aches, abdominal pain and nervousness. She was found to have "splinter" hemorrhages of the finger nail beds, conjunctival petechiae, a grade II pulmonic systolic murmur, rales at the lung bases, splenic and hepatic enlargement, and a temperature spiking to 103°F. The white blood count was 21,000 with 30 per cent eosinophils; the urine contained albumin, granular and hyaline casts, and a few red and white blood cells. Chest x-rays showed a pulmonary edema pattern, with a small area of left upper lobe consolidation; six days later there was extensive "bat-wind" edema with small nodules in the right costophrenic area; there was also a small pleural and a pericardial effusion. Biopsy of calf muscle was reported perivascular inflammation, and of skin as chronic dermatitis. Cortisone resulted in excellent subjective response. Fever stopped, strength improved, but the splenomegaly and hepatomegaly persisted. She was discharged as improved.

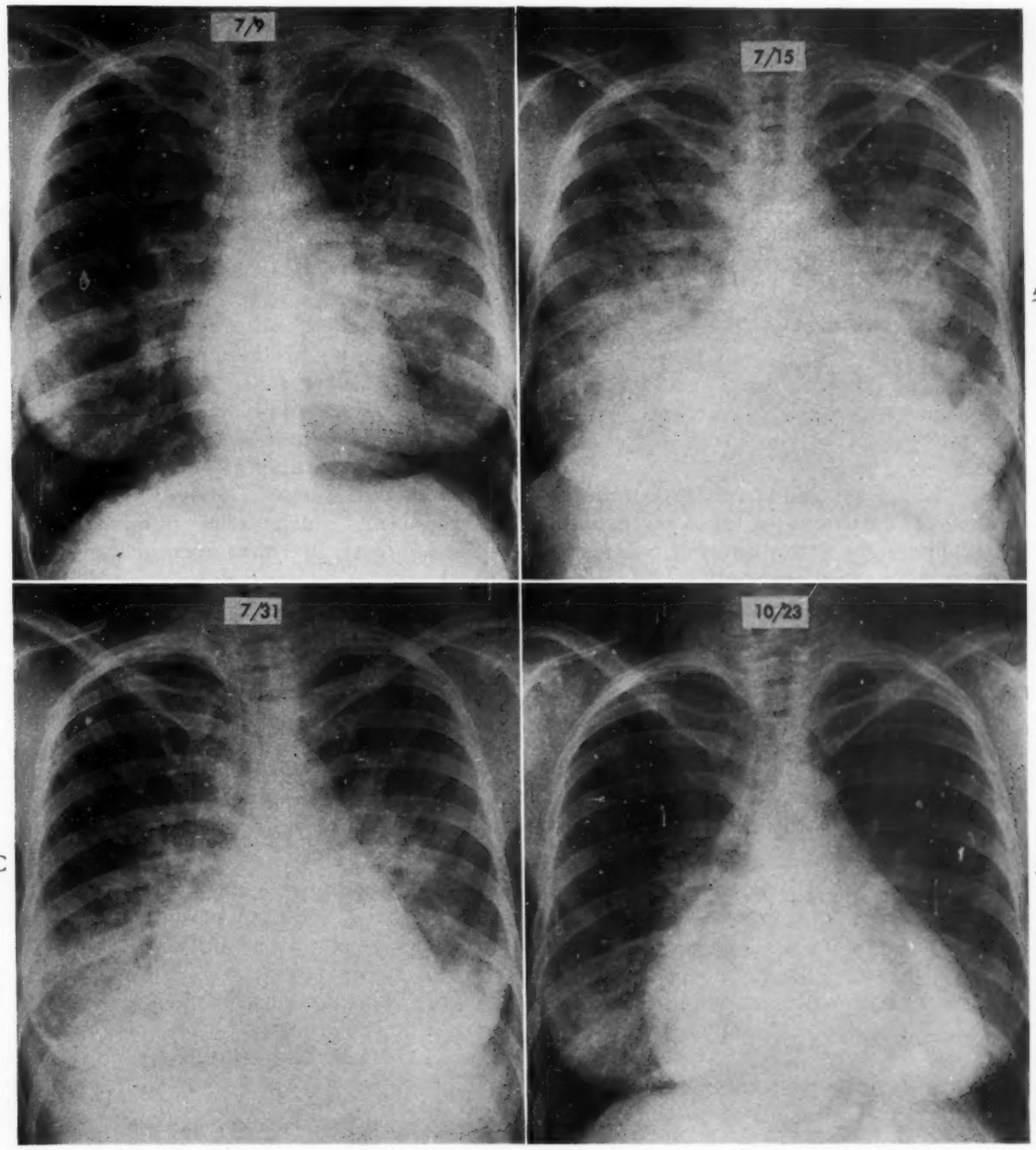
DISSEMINATED LUPUS ERYTHEMATOSUS

Disseminated lupus erythematosus, or systemic lupus erythematosus, is a disease most commonly seen in women, and in the ages of twenty to forty. It is characterized by a cutaneous eruption, most often in the form of discoid lesions—with a butterfly distribution over the nose and cheeks—along with varying degrees of visceral manifestation, notably in kidneys, heart, spleen and lungs. The skin lesion is frequently photosensitive, being made worse by sunlight or ultraviolet light or such light-sensitizing drugs as the sulfonamides. Patients may show fatigue, arthralgia and fever. The laboratory findings include leukopenia, an elevated sedimentation rate, a "telescopic" urinary sediment and the presence of so-called lupus erythematosus cells.[15] These lupus erythematosus cells, found only in this disease, are seen in various preparations of blood and bone marrow and are reportedly large leukocytes containing phagocytosed material resulting from lysis of the nuclei of other leukocytes.

Pathologically, there is predominant involvement of the smaller arteries and arterioles. Polyserositis is common, with pericardial lesions the most frequent. In the heart itself, lesions predominate in the valvular structures and the mural endocardium. The kidneys, when involved, tend to be enlarged. The glomerular vessels show the so-called "wire-loop" appearance due to eosinophilic thickening of the vascular loops within the glomeruli. Occasionally, the renal changes resemble those of glomerulonephritis or periarteritis nodosa. The spleen shows microscopic involvement in at least half of the cases (periarterial fibrosis). The lymph nodes are said also to be frequently involved, showing "free hematoxylin-staining bodies."*

Roentgenologically, findings may be noted in the urinary and respiratory tracts. In the urinary tract, when a case of hypertension

* Klemperer, P. et al. Cytochemical changes of acute lupus erythematosus. *Arch. Path.*, 49: 503–516, 1950.



5A 5B 5C 5D

FIG. 5. Case I. S. Periarteritis nodosa, with pulmonary "edema," small nodules and patchy densities and pleural and pericardial effusions. Female, aged thirty-one, with asthma, muscle, joint and abdominal pains, conjunctival and nail-bed petechiae, enlarged liver and spleen, spiking fever, leukocytosis with 30 per cent eosinophilia, and telescopic urinary findings. Muscle biopsy consistent with diagnosis. Partial response to cortisone. A, moderate pulmonary "edema" with small area of consolidation in left upper lobe. B, six days later extensive "edema," small nodules in right costophrenic area and small right pleural and pericardial effusion. C, sixteen days later, after being on cortisone for about one week. Lungs improved but pericardial effusion slightly increased. D, three months later; residual prominence of pulmonary markings, and increased pericardial effusion.

shows unusually large kidneys, the possibility of disseminated lupus erythematosus rather than a chronic glomerular nephritis must be considered. Patients with the latter condition tend to have small or contracted kidneys.

Pulmonary involvement is remarkable for its frequency and its atypical course. Rakov and Taylor,[24] and Foldes[11] describe a chronic interstitial pneumonitis which leads to atelectasis (due to interstitial edema and inflammation

resulting in obliteration of some alveoli)—termed atelectasizing pneumonitis. These lesions are regarded as different from the ordinary pyogenic and fibrinous types of bronchopneumonia which so frequently complicate the terminal stages of lupus erythematosus.

TABLE II

CHEST ROENTGEN FINDINGS IN THIRTY-FIVE CASES OF DISSEMINATED LUPUS ERYTHEMATOSUS

No evidence of disease	12
Evidence of disease	23
Cardiac enlargement	5
Pericardial effusion	5
Pleural effusion	15
Pulmonary changes (Accentuated markings, nodules, densities or edema)	11

Thorell[30] reviewed the roentgenograms of fifteen cases of disseminated lupus erythematosus and found eight with pleural or pulmonary parenchymal changes, or both. The pleural effusions were generally small; the pleural thickening more or less irregular. These pleural changes varied in extent in relatively short periods of time. The parenchymal changes consisted of small areas or patches of increased density, mostly subpleural, especially in early and moderately advanced cases. (He used different oblique projections to bring out the subpleural location of the lesions.) He believed that a combination of pleural and subpleural change ought to lead to the correct diagnosis even if the changes in themselves were not characteristic.

In our experience pleural and pericardial effusions were the most common findings in this group. The pulmonary parenchymal changes varied from localized accentuated markings, nodules and patches to extensive edema.

We have reviewed the records of thirty-eight cases, in thirty-five of which chest films were available. (Table II.)

In these cases the pulmonary changes consisted of accentuated basal bronchovascular markings in two instances, of nodular or patchy pulmonary densities (edema?) in seven instances, and of diffuse pulmonary density (edema) in two instances.

As far as other anatomic sites are concerned, our roentgenologic findings are limited. In one case hepatomegaly was reported; in two cases ascites was noted. No gastrointestinal lesions were detected. In one case slight osteoporosis of the hands was noted. While many of our patients had clinical evidence of joint disorder, none were so reported roentgenologically (largely because examination was not regarded as necessary by the ward physician).

Biopsy or necropsy material compatible with the diagnosis of disseminated lupus erythematosus was available in twenty-four of the thirty-five cases. In two cases biopsy reports were negative. It is currently believed that search of the blood or bone marrow should replace biopsy, being an easier and more accurate method of diagnosis.

The following are illustrative case reports:

Case N. F. (Fig. 6), aged nineteen, white, had a facial rash of butterfly shape, fever, joint pains for six months and generalized edema (nephrotic syndrome?) for four weeks. Chest films showed a small amount of fluid in the costophrenic sulci. This minimal bilateral effusion, without other roentgen evidence of chest disease, is one of the more suggestive findings of disseminated lupus erythematosus in patients with concomitant clinical findings. Biopsy was not performed.

Case T. S. (Fig. 7), a thirteen year old boy, entered with high fever and weakness, splenomegaly and lymphadenopathy of two months' duration and a butterfly facial rash of one month's duration. The initial chest film showed slightly accentuated pulmonary markings. Three days later bedside films showed a bilateral pneumonitis, and six days later the patient died. Autopsy showed a disseminated lupus erythematosus and also a bilateral atypical lobar pneumonia with features suggesting the anaphylactic pneumonia of Rich. This is a type reported by Rich as occurring in rheumatic fever and sulfonamide sensitivity.

Case F. R. (Fig. 8), a school girl, aged fifteen, developed painful, swollen joints and fever. Chest roentgenograms showed a "water-bottle" shaped heart suggesting pericardial effusion (this was confirmed by roentgenoscopy); she also had minimal bilateral pleural effusions. Examination eighteen days later showed a marked decrease in heart size; the pleural effusions were unchanged. The clinical diagnosis was disseminated lupus erythematosus. No biopsy was performed.

Case R. P. W., a thirty-six year old white man, gave a history of chorea at the age of twelve, and had developed a butterfly rash two and one-half years ago, then hematuria and fever, weakness and fatigue. Ten months ago he

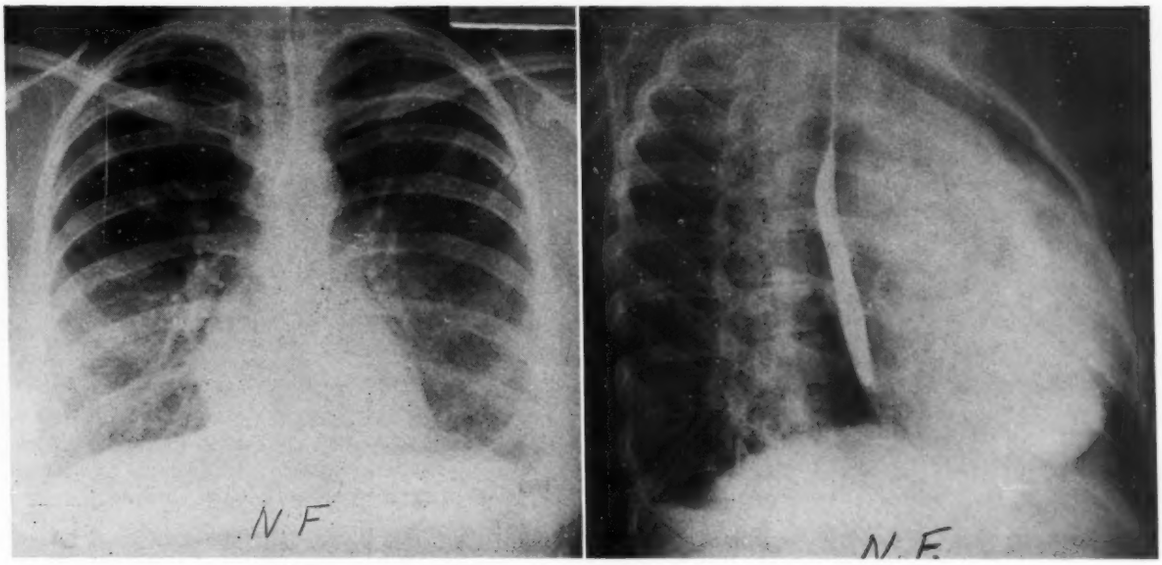


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FIG. 6. Case N. F. Disseminated lupus erythematosus, with small bilateral pleural effusions. White, female, aged nineteen, with facial rash, fever and joint pains for six months. "Nephrotic syndrome" for four weeks. A, bilateral pleural effusions. B, right oblique view; fluid seen posteriorly. Similar findings were present in left oblique view. (Courtesy of *Am. J. Roentgenol.*)

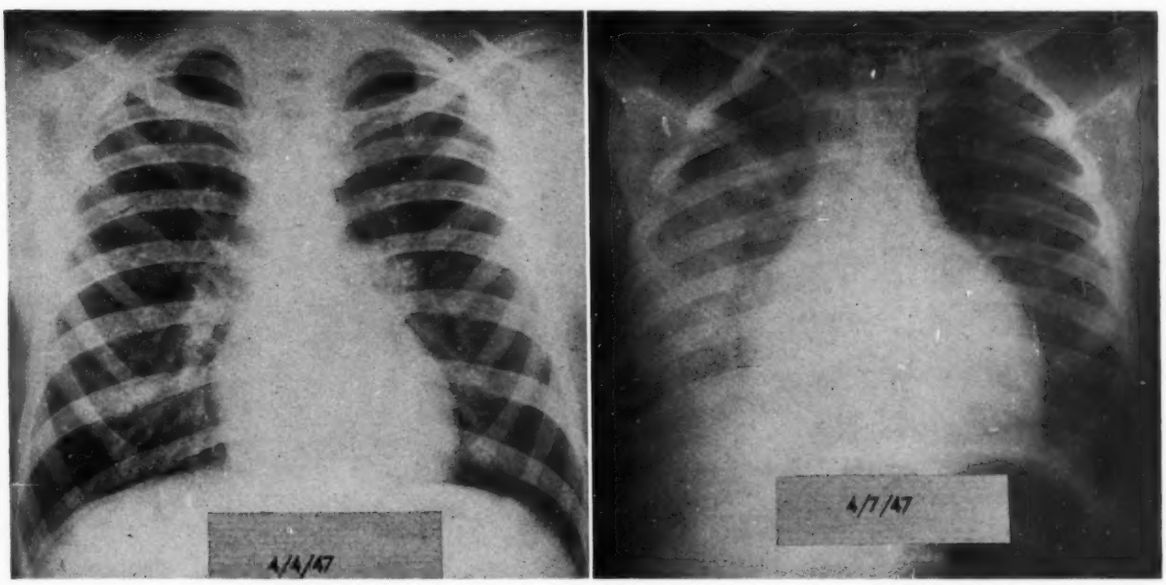

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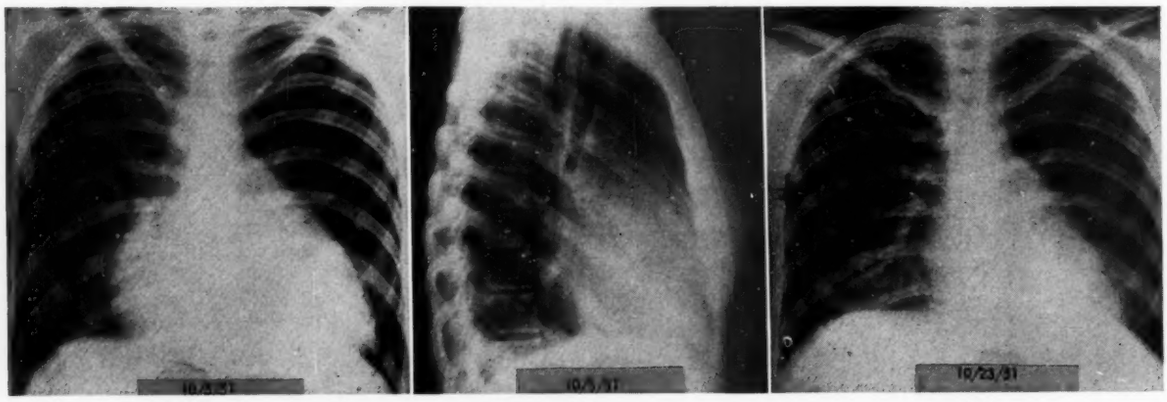
FIG. 7. Case T. S. Disseminated lupus erythematosus, with development of atypical pneumonia or pneumonitis. White, male, aged thirteen. Fever, weakness, splenomegaly and lymphadenopathy for two months. Butterfly facial rash one month. A, slightly accentuated pulmonary markings. B, bedside film. Consolidation right (? pneumonia); patchy basal densities on left (? pneumonitis). Patient died six days later. Autopsy showed disseminated lupus erythematosus and bilateral atypical lobar pneumonia, with features suggesting anaphylactic pneumonia. (Courtesy of *Am. J. Roentgenol.*)

was hospitalized and a diagnosis of disseminated lupus erythematosus and aortic insufficiency was made. The blood pressure was 170/96. Recently marked orthopnea and minimal edema developed. The blood pressure varied from 160/90 to 200/110. Roentgenograms ten days before death showed cardiac enlargement. The patient died in cardiac failure. Autopsy showed a chronic glomerular nephritis (without evidence of disseminated



8A 8B 8C

FIG. 8. Case F. R. Disseminated lupus erythematosus showing marked pericardial effusion and minimal pleural effusion. White, female, aged fifteen. Painful swollen joints and fever. A, "water-bottle" heart due to pericardial effusion; small bilateral pleural effusions. B, lateral view. C, marked decrease of pericardial effusion; minimal pleural effusions persist. (Courtesy of *Am. J. Roentgenol.*)

lupus erythematosus) and spleen lesions consistent with disseminated lupus erythematosus. There was microscopic evidence of active rheumatic lesions. This case again showed a combination of "collagen" diseases.

DERMATOMYOSITIS

Dermatomyositis is the rarest of the collagen disease group and is characterized by a nonsuppurative inflammation of the skin, subcutaneous tissues and skeletal muscle. There also may be inflammatory changes in the vessels, myocardium and muscles of deglutition. Little is known about the roentgenologic features. We have had only one autopsy proved case, this showing a cloudy swelling of the myocardium and a congestive failure. Chest roentgenograms taken a year before death showed the heart to be slightly larger than normal, but several weeks before death the heart vessel shadow was normal in size. The lungs were clear.

SCLERODERMA

Scleroderma is a polysystemic disease, with fairly well known roentgen findings. (Table III.) Large series of cases have been reported in the literature, one of the most comprehensive, from the roentgenologic viewpoint, being that by Pugh.[23] Based on this material plus our own experience we believe that Table III summarizes the more important roentgenologic changes in this disease.

We have reviewed ten microscopically proved cases of scleroderma in our hospital, five of

TABLE III

SUMMARY OF THE ROENTGENOLOGIC FINDINGS IN SCLERODERMA

A. Gastrointestinal tract:
   1. Esophagus
      a. Loss of peristalsis due to rigidity
      b. Variable degrees of dilatation
      c. Occasional narrowing of distal esophagus
      d. Occasional shortening of esophagus
   2. Stomach:
      a. Peristalsis may be decreased
      b. Hiatus hernia may develop
   3. Small intestine:
      a. Peristalsis decreased or absent
      b. Widening, especially of duodenum and jejunum; this may be segmental
   4. Colon:
      a. Peristalsis decreased
      b. Segmental narrowing
B. Lungs:
   1. Diffuse or localized fibrosis
   2. Diffuse or localized nodulation
   3. Subpleural "cystic disease" (basal)
   4. Calcification (calcinosis)
C. Heart:
   1. Decreased amplitude or excursion
   2. Heart may be small, normal or large
D. Phalanges:
   1. Absorption of distal phalanges in advanced cases
   2. Occasional increased density of phalanges
   3. Occasional synostosis, distal and middle phalanges
E. Soft tissues:
   1. Calcinosis—fairly frequent and often accompanies phalangeal absorption
      a. Varies from "sand" to plaques
      b. Usually in pressure areas: fingertips, elbows, ischial tuberosities
      c. Usually seen only where there is cutaneous sclerosis
F. Teeth
   1. Uniform widening of the periodontal spaces (reported in 7 per cent of cases)

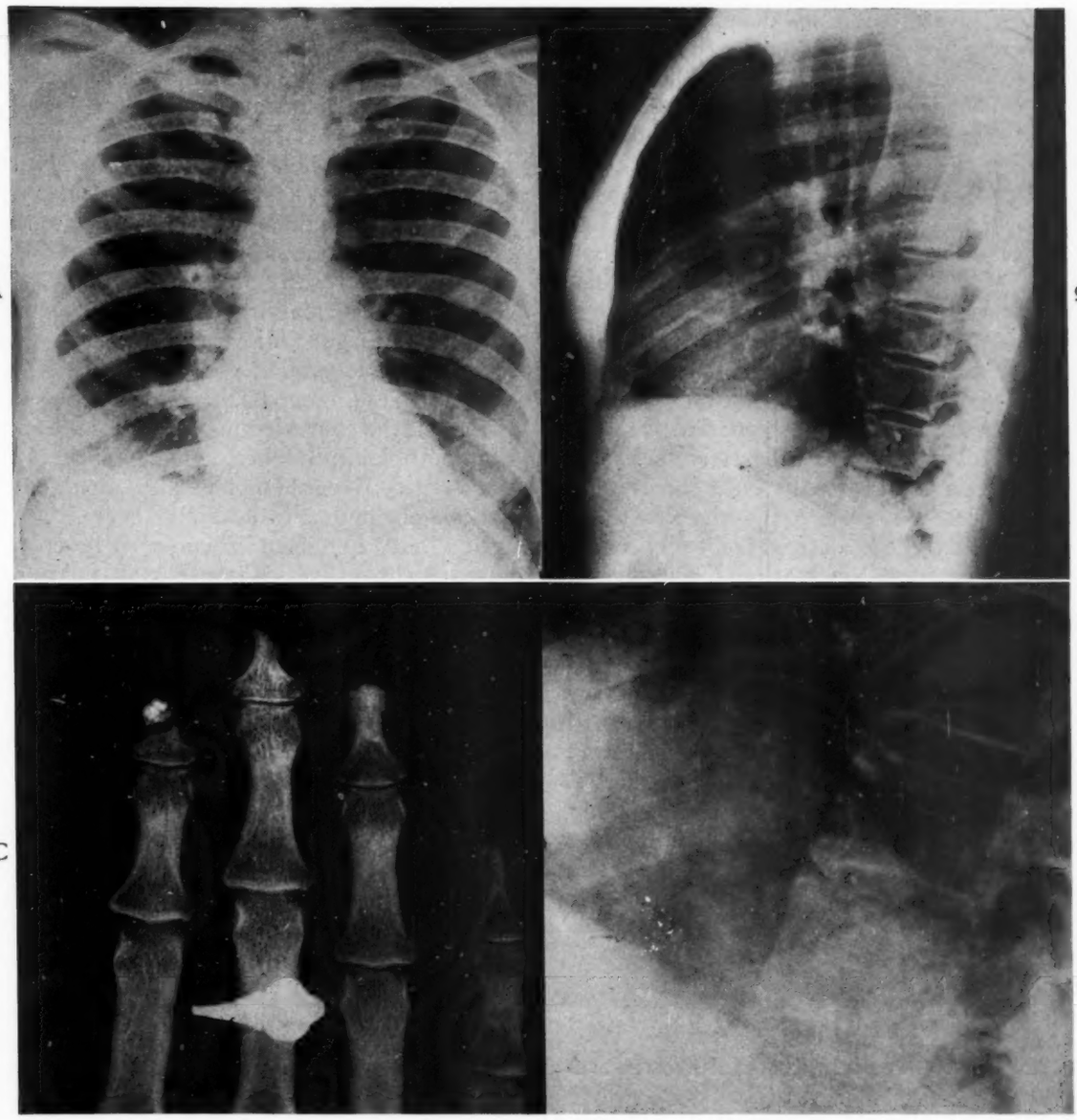


FIG. 9. Case D. R. Scleroderma, with "cystic" disease of the lung bases. Negro, female, aged thirty. Scleroderma for twelve years. A, mottled radiolucencies (? cysts) in lung bases. B, lateral view. C, tuft absorption and calcinosis. D, detail view of "cystic" appearance; the lesions are small, resulting in a "spongy" appearance on the films. (Courtesy of *Am. J. Roentgenol.*)

which showed some degree of small intestinal abnormality. One of the ten cases showed pulmonary disease.

Case R. L. P., a seventy-five year old Chinese man, had weight loss (from 150 to 116 pounds), marked weakness, dyspnea, ankle edema and a cough productive of white, frothy phlegm. The skin of the face and fingers appeared drawn, tense and shiny. He died of a ruptured diverticulum (diverticulitis) of the mid-ascending colon eight days after starting on corticotropin. Chest roentgenograms five months before death showed minimal prominence of the lower lobe pulmonary markings and slight cardiac enlargement. Examination three days before starting corticotropin showed hazy widening of the pulmonary markings throughout both lung fields, with a few areas of small (2 to 3 mm.) hazy nodules along the course of these markings. The changes were more evident in the right upper lobe, where one patchy density (1.5 by 3 cm.) was also present. The left costophrenic sulcus was blunted by fluid.

Among several clinically diagnosed cases of scleroderma, we have seen one with subpleural cystic changes. Case D. R. (Fig. 9), a thirty year old Negro woman, had definite scleroderma for twelve years. Chest roentgenograms showed a peculiar "spongy" appearance in the bases, presumably due to cystic changes, as described by Getzowa[13] in two cases. These were cases interpreted as examples of "cystic and compact pulmonary sclerosis." The "cysts" varied from pinhead size up to 1.5 cm. in diameter. Only one showed concomitant extensive fibrosis. The cyst-like changes were believed to be due to a disappearance of alveolar tissue in the lung secondary to lysis of the alveolar walls and progressive sclerosis. This sclerosis is reportedly on a basis of a "hyaline process involving the alveolar walls, accompanied by the disappearance of capillaries, superimposed on a generalized, diffuse simple fibrosis of the alveolar walls."

Shuford et al.[28] found that six of thirty-seven patients clinically diagnosed as scleroderma had abnormal chest x-rays. One had pulmonary edema (as a terminal phenomenon). Five had widespread linear reticulated infiltration, more marked in the lower halves of the lung fields. They believe that differentiation from other diseases causing diffuse interstitial pulmonary fibrosis is difficult, if not impossible. The pneumoconioses classically have a nodular rather than linear type of fibrosis, with emphysema (which is absent in scleroderma). Hilar adenopathy is frequent in sarcoid but rare in scleroderma.

RHEUMATIC FEVER AND RHEUMATOID ARTHRITIS

We have reviewed some of the recent literature on rheumatic fever and rheumatoid arthritis, but have not analyzed in detail our cases of these diseases. Acute rheumatic fever is regarded as a collagenous degeneration which localizes selectively in the heart. The changes may be found in many other organs, as shown by the arthritic, dermal, serosal, intestinal and pulmonary manifestations of the disease. In acute fulminating form, pulmonary complications are reportedly found in as high as 50 per cent of cases.[14] "Rheumatic pneumonitis" has no specific diagnostic features, in our experience. Pericarditis is not uncommon. The involved joints tend to show only articular and periarticular swelling.

While the foregoing has been our own experience in connection with so-called "rheumatic pneumonitis," many writers do believe that such an entity is common and diagnosable. For example, Bland and Jones[3] mention that "areas of consolidation in the lungs, peculiar in their clinical behavior, occur in rheumatic pneumonia." Chancey[4] describes three types of rheumatic pneumonitis: a primary acute type which may be the presenting sign of rheumatic fever, a secondary acute type which occurs in the established case of rheumatic fever and a "subclinical pneumonitis" which is often discovered accidentally in patients with subacute, monocyclic rheumatic fever.

Part of the confusion may arise from the fact that pathologically there appears to be a distinct entity. Neubuerger et al.[22] reviewed the pathologic findings on sixty-three cases of active and quiescent rheumatic fever, and noted eight in which there was pulmonary inflammation with distinctive microscopic features. These included peculiar granulomas in the alveolar ducts and alveoli, focal alveolitis with necrosis, mononuclear cell exudation and septal cell proliferation. The rheumatic pulmonary granuloma has been referred to as the Masson body, allegedly similar to the Aschoff body which is found in the heart. Seldin et al.[27] believe that there is little difficulty in microscopically distinguishing rheumatic pneumonia from bacterial or viral forms.

Rheumatoid arthritis is frequently complicated by myositis, neuritis and arteritis, as demonstrated in 70 per cent of muscle biopsies by Traut[31] and Campoine. Traut also states that these biopsies show aggregates of lymphocytes, epitheliod cells and plasma cells somewhat similar to those in dermatomyositis, lupus erythematosus and scleroderma. Pericarditis is the only unusually frequent cardiac complication, being especially common in juvenile rheumatoid arthritis (Still's disease). In addition, a pneumonitis and pleuritis may occur along with the inflammatory reaction in the joints but is rare. The roentgen findings in the bones and joints of patients with rheumatoid arthritis are well known.

While we have seen no convincing evidence of specific pneumonitis in connection with rheumatoid arthritis, Ellman and Ball[10] report three cases in which they believe there was such relationship. The roentgen findings in one case consisted of "fine reticulation" with chronic bronchopneumonia. In one there was

bilateral patchy consolidation in the bases, with "reticular shadows" in the middle thirds of the lungs. In the third case there was widespread "heavy reticulation and miliary mottling." The first and second cases were autopsied and showed interstitial pneumonitis and terminal bronchopneumonia; the pneumonitis had well marked fibrinoid necrosis between the lung alveoli, similar to that described in other collagen diseases.

COMMENTS

Collagen diseases constitute an interesting group of disorders—from the clinical side because of their diagnostic and therapeutic challenge, from the pathologic viewpoint because of recent interest in the intercellular substances, and from the roentgenologic viewpoint because of their widespread but unfortunately non-specific nature.* The latter is particularly true of the pulmonary manifestations of the collagen diseases. We believe, however, that diagnostic possibilities, slim as they are, depend on an awareness of these conditions, plus a knowledge that the patient has a polysystemic disease. It is desirable that radiologists, as clinicians, be able occasionally to suggest the consideration of one of these diseases, on logical grounds, and be cognizant of the further studies, clinical, laboratory or pathologic, required to confirm the diagnosis.

From a review of our roentgenologic findings, we believe that pulmonary changes occur more frequently in periarteritis nodosa and disseminated lupus erythematosus than one would gather from the literature. Further, from a survey of the histories of over eighty patients with established or clinically diagnosed collagen disease, we have the distinct impression that peptic ulcers occur with relatively greater frequency in these conditions than in the rest of the hospital population in general.

In studying a patient for possible collagen disease it is desirable that particular attention be paid to the following structures: (1) the skin and muscles; (2) the heart and pericardium; (3) the lungs and pleura; (4) the abdomen and intestinal tract; (5) the kidneys; and (6) the bones and joints.

* At the same time, it is believed that the term "collagen" disease is one of high abstraction, to be modified or abandoned as soon as the etiology and fundamental nature of these conditions becomes established.

The skin and muscles may show microscopic evidence of involvement in any of the four types of collagen disease discussed in this paper.* Histopathologic changes are reportedly fairly decisive in all except dermatomyositis, about which not enough is yet known; they are said to be most clear-cut in periarteritis, but there is divergence of opinion as to their clarity in scleroderma.

The cardiac and pleuropulmonary changes are many and non-specific. Pericardial effusion, cardiac enlargement, pleural effusion, pulmonary nodular changes and variable degrees of pulmonary edema or fibrosis may occur. These changes may be reversible.

Abdominal distention, with paralytic obstruction, may occur in the first two conditions. Renal enlargement may also be seen in these two (periarteritis nodosa and disseminated lupus erythematosus).

The intestinal tract changes are most conspicuous in scleroderma, notably in the esophagus and small intestine (variable degrees of rigidity, dilatation and narrowing occur in about 50 per cent of cases).

The articular and osseous changes occur in periarteritis nodosa, lupus and especially scleroderma. Roentgenologically, they are characteristic only in the latter condition. Calcinosis is also confined largely to this disorder.

SUMMARY

We have reviewed currently accepted criteria concerning the pathology, classification and diagnosis of the so-called collagen diseases.

We have reviewed our personal experience with the roentgenologic aspects of these diseases, and have summarized our findings in thirty-one cases of polyarteritis; thirty-five cases of generalized lupus erythematosus; one case of dermatomyositis; and twenty-five cases of scleroderma.

In this entire group pathologic material was available for study in sixty-four cases and was interpreted as "positive" for the particular disease in question in fifty-four instances.

It is believed that awareness of the roentgenologic findings in these disease entities will give the clinical radiologist greater opportunity for reaching or suggesting the correct diagnosis in everyday practice.

* Periarteritis nodosa, disseminated lupus erythematosus, dermatomyositis and scleroderma.

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The Mycotic Infections of the Bronchial-Pulmonary Tract

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THE study of the mycotic infections of the lungs makes up one of the most interesting chapters in the field of non-tuberculous diseases of the chest. In their close resemblance, both as to the symtomatology and radiologic findings with that of tuberculosis, the pneumomycoses offer a challenge to the diagnostic ability of the internist, chest specialist and radiologist. Since the tendency today in tuberculosis is to lay even greater stress on methods of investigation which will enable an early diagnosis to be made, although it be presumptive only, there will be correspondingly a greater delay in carrying out diagnostic procedures which are extremely essential in the differential diagnosis of the two conditions.

Clinically, these pulmonary infections are of interest mainly because of their resemblance to tuberculosis, and undoubtedly they occur more often than is generally suspected or recognized. As in tuberculosis, the chief symptoms are cough, loss of weight, night sweats, fever, dyspnea, purulent sputum and hemoptysis. Moreover, the physical signs are compatible with a tuberculous infection except that in general, tuberculosis has a predilection for the apical regions, whereas the mycoses invade chiefly the hilar, middle and lower pulmonary fields. From a radiologic examination no definite help can yet be expected except that atypical shadows in radiograms of the lungs suspected of being tuberculous should promote more decisive bacteriologic investigation and the carrying out of a tuberculin test which, if negative, may prove of some diagnostic value.

During the past decade numerous articles have appeared in the literature describing the various forms of pulmonary mycoses. It is a significant fact that in many of the reported cases the diagnosis was either established very late in the course of the disease or was confirmed at autopsy. Because of the general delay in the diagnosis the mycotic infections carry a very high mortality. During the past year the author has seen several fatal cases of chronic pneumomycoses in which a tentative diagnosis of tuberculosis had been made previously. In spite of the fact that the sputum in these patients had been repeatedly negative for tubercle bacilli, not until very late in the course of the disease had any thought been given to the possibility of this type of infection. The sooner it is realized that the final diagnosis of the mycoses rests with the laboratory, which should be employed as soon as possible, the greater will be the opportunity to effect a complete cure in many of these cases.

HISTORICAL CONSIDERATION

A search of the available literature dealing with the subject of fungi and fungous disease reveals that the science of mycology was in existence long before that of bacteriology. It may be said to have begun in the days of Charles II when Hooke, in 1677, constructed a magnifying lens with which he examined the yellow spots so often present on the leaves of the damask rose.[1] He found that they consisted of filamentous fungi which he believed arose from decaying matter by a process of spontaneous generation. This initial discovery soon was followed by much work, and a considerable number of published articles appeared in the scientific periodicals of the time. However, it was not until the discovery of the thrush fungus by Lagenbeck in 1839 that parasitic fungi in man began to attract attention. In 1843 Charles Robin classified this fungus as Oidium albicans. In the same year (1839), soon after Lagenbeck announced his discovery, Schonlein found another important fungus, the fungus of Flavus. In 1844 the fungus of ringworm was discovered by Gruby, and two

years later Eichstedt discovered the fungus of pityriasis versicolor.

The science of mycology continued to attract attention until the great discoveries by Pasteur[2] and Koch in the field of bacteriology. This immediately brought the study of bacteria to the foreground and mycology was placed in the background where it has remained until recent years.

MYCOLOGIC AND CLINICAL CLASSIFICATION

Since the time of Robin,[2] Wernicke,[3] Busse,[4] Gilchrist and Stokes,[5] Rixford,[6] Montgomery and Ormsby,[7] and Castellani and Ashford,[8] many attempts have been made to classify and identify the fungi pathogenic for man. In recent years Jacobson,[2] Dodge,[8] Stovall,[9] and Smith and McBryde[10] have added greatly to our knowledge of this subject. In a study of the fungi one finds so much disagreement among students of the subject regarding the botanical and pathogenic classification that it seems best to consider these organisms in connection with the disease that they are known to cause.

For the purpose of clinical study the pneumomycoses may conveniently be divided as follows:

Yeast-like fungi: In their simplest form these reproduce by budding and may form a mycelium. This group includes Saccharomyces, Monilia, Torula histolytica, Oidium, Blastomyces, Coccidioides immitis, Histoplasma capsulatum and Sporothrix.

Mold-like fungi: The fungi of this group are characterized by the presence of a stalk with a spore-bearing head which forms fruiting branches and which support specialized cells called conidia. This group includes Aspergillus, Penicillium and Mucor.

Higher bacterial forms: The fungi of this group are characterized by branching mycelia, which break up into segments as conidia with clubbed ends and radiating threads. This group includes Actinomycete (acid fast and non-acid fast; anaerobic and aerobic), Nocardia and Streptothrix.

BRONCHOMONILIASIS

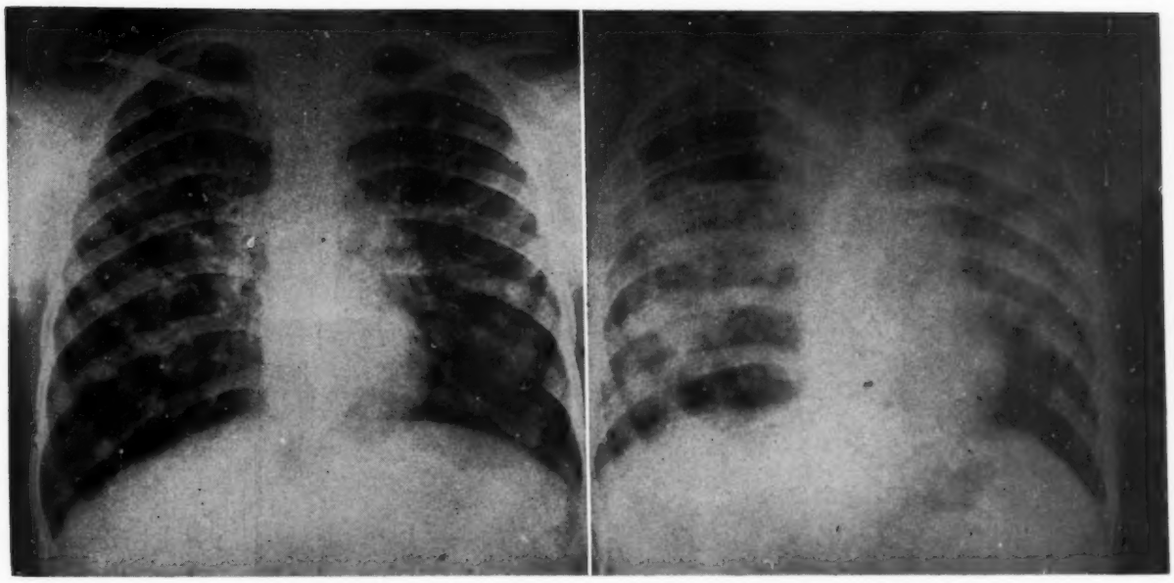
Monilia infection of the lungs represents chronic and slowly progressive inflammation in which pathogenic monilia is understood to play a cardinal etiologic role. The pulmonary form is caused by a yeast-like fungus which falls under the classification of Monilia albicans. The organism is oval in shape and measures from 3 to 10 microns in diameter. It reproduces by budding and produces septate hyphae which intertwine to form a mycelium.

The condition was first recognized by Castellani[12] in 1905 among the tea workers of Ceylon and for a time it was thought to be a tropical or subtropical disease. Numerous cases have since been reported from various parts of the world. The first instance of infection to be observed in this country was the case reported by Boggs and Pincoff in 1915[12] in the *Bulletin of the Johns Hopkins Hospital.* Bronchopulmonary moniliasis is no longer considered a rare disease, although the diagnosis must be made with extreme caution since the organism is often found in association with many types of bacteria in common respiratory infection, particularly in the sputum of patients suffering from pulmonary tuberculosis. The organism is extremely saprophytic and may, if the pulmonary tissue resistance becomes markedly lowered, find fertile soil to completely overgrow the primary bacteria.

During the past several years it has been well known that broad-spectrum antibiotic therapy has been responsible for a further increase in the incidence of gastrointestinal and pulmonary moniliasis. This so-called secondary fungous infection is due to the fact that this type of therapy may remove both gram-positive and gram-negative organisms yet leave in their wake an overgrowth of resistant bacteria and yeasts. A rather distressing number of fatal fungous infections complicating antibiotic therapy have already been reported in the recent literature.[34] Today, we have come to realize that one of the hazards of antibiotic therapy, in the dislocation of the bacterial population, may lead to serious secondary infection.

Mode of Infection. Monilia is resistant to drying and, like the tubercle bacilli, may live indefinitely in dust and a dry environment. The occurrence of this condition among the tea tasters and the coolies working in the dust of tea factories in India, among the pigeon feeders who handle dried bird food and among the peddlers of dried fruit and straws in Egypt strongly points, as in tuberculosis, to inhalation as the most probable means of transmission.

Bronchomoniliasis may be recognized in one of three forms, the mild, the intermediate, and the severe.



1 2

FIG. 1. Generalized pulmonary moniliasis in a ten year old boy. This is the youngest patient with moniliasis ever seen by the author.

FIG. 2. Pulmonary moniliasis in a twenty-five year old man, having a fatal termination.

In the *mild* type the patient merely complains of a slight cough without temperature elevation or the appreciable physical signs of pulmonary disease. The sputum is scanty and mucoid in character. The diagnosis usually made at this time is that of chronic bronchitis. As the condition progresses the cough becomes more marked, the sputum increases in amount and the patient begins to complain of asthmatoid-like wheezing. In many instances the diagnosis is changed from that of chronic bronchitis to that of asthmatic bronchitis and eventually these patients are referred to the allergist for treatment.

In the *intermediate* form the clinical symptoms and physical signs are more exaggerated. There is a persistent low grade fever, the cough is more troublesome and the entire picture may closely resemble early pulmonary tuberculosis.

The *severe* form of the disease is chronic in type and usually terminates fatally. The pulmonary involvement may be unilateral or bilateral and there is frequently an associated pleural involvement. The general clinical picture is that of pulmonary tuberculosis. In this type, as in the intermediary form, there is usually a yeast-like odor to the sputum. This is a very important clinical symptom and should be closely watched for in sputum from chronic pulmonary cases, in which there is repeated absence of tubercle bacilli.

The sputum of patients suffering from bronchomoniliasis is usually copious and has been described by various authors as "curdy," "lumpy" and "gruel-like." Not infrequently the sputum is hemorrhagic.

Except that this disease usually involves the middle and lower pulmonary fields, the radiologic studies are not distinctive and simply reveal diffuse pulmonary infiltration with or without cavity formation. The entire radiologic picture is generally interpreted as: (1) advanced pulmonary tuberculosis; (2) suppurative pneumonitis; (3) mycotic pneumonia. (Figs. 1 and 2.)

Diagnosis and Treatment. The final diagnosis of bronchomoniliasis rests with the laboratory,[13] which should be employed as soon as possible. The history of chronic pulmonary infection, with repeated absence of tubercle bacilli from the sputum, should lead one to consider the possibility of a mycotic infection. A very important clue is sometimes given by the yeast-like odor of the sputum. It is generally agreed by the medical mycologists that M. albicans is the only species of genus Monilia which is pathogenic to man, and should be regarded as responsible for the development of pulmonary moniliasis. Sputum from suspected cases of tuberculosis should be examined routinely for fungi. If the first examination reveals no tubercle bacilli, the sputum should

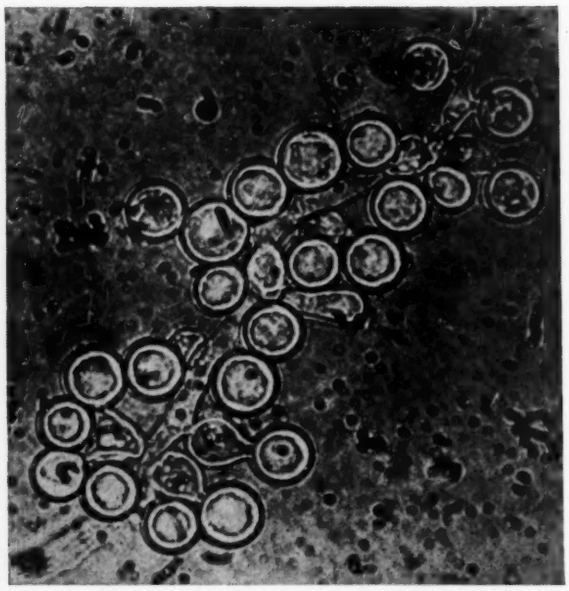


FIG. 3. Chlamydospore formation in Monilia albicans massed along the hyphae. (Courtesy of Jacob H. Swarts, M.D., Elements of Medical Mycology. New York, 1943. Grune & Stratton.)

then be cultured on Sabouraud's media. In hospitals and sanatoriums where a trained bronchoscopist is available it is recommended that the sputum to be cultured be obtained by bronchoscopic aspiration, thus avoiding the possibility of oral contamination. (Fig. 3.)

Potassium iodide is the drug of choice in this condition, as it is for many of the other mycoses. The best results are obtained when the drug is given in small doses at the beginning of treatment. The author prescribes 5 gr. three times daily and gradually, by the daily addition of 3 gr., the dosage may be brought up to 60 to 80 gr. three times daily. If, during the oral administration, the patient becomes nauseated and unable to retain the drug, it is temporarily discontinued and 10 cc. of a 2 per cent sodium iodide solution is given intravenously for a period of several days. Ethyl iodide inhalations are another method of iodide therapy and excellent results have been obtained by using this method alone in preference to the use of the oral potassium iodide administration.

In the mild bronchial form excellent results are sometimes obtained by the intratracheal instillation of a 40 per cent iodized oil. One patient treated by the author[13] could not tolerate the oral administration of potassium iodide. Therefore, four instillations of 5 to 10 cc. of lipiodol® were given at weekly intervals. Aerosol inhalations of an antifungal drug such as zephiran® chloride in the strength of 1:3000, using 3 to 5 cc. three times daily has proved very effective in the bronchial allergic form of moniliasis. Acti-dione,® a by-product in the manufacture of streptomycin, has also been reported of some value in the treatment of the pulmonary form of moniliasis. Stovall[9] and others recommend the use of gentian violet given intravenously in the dosage of 5 mg./kg. of body weight.

Martin and Smith[14] have called attention to the similarity of many of the pathologic and clinical features of the various pulmonary mycoses to tuberculosis, and suggest that an allergic state similar to the hypersensitiveness seen in tuberculosis would not be surprising. They further call attention to the value of skin testing with the causative fungus before any form of therapy is considered. Iodides are given cautiously and only if the patient shows a negative or weakly positive skin reaction. If the patient exhibits a marked skin reaction, an attempt is made to reduce the sensitivity by vaccine therapy before iodides in any form are given. From their experience they have found iodides distinctly harmful if the patient is strongly allergic.

At the present time a vigorous search is underway to discover newer antifungal agents. Many antifungal antibiotics have been reported in the recent literature for the treatment of moniliasis. Thus far they have not found widespread use because of inherent toxicity or other unfavorable properties. As these agents undergo a more thorough study, they may prove clinically more acceptable. Mycostatin,[35] one of the first antifungal antibiotics to be developed, is very effective in the treatment of intestinal moniliasis resulting from protracted oral treatment with antibiotics against intestinal bacteria. The drug is given orally in dosage of 500,000 unit tablet, three times daily. If intestinal fungi, as shown by stool examination, are not adequately suppressed, the dosage may be doubled. Unfortunately, because the drug can only be administered orally and is so poorly absorbed in the intestinal tract, it cannot be depended upon for systemic effects. Candidin[36] and candicidin,[37] antifungal antibiotics produced by Streptomyces viridoflavus, have been shown to exhibit a marked inhibitory effect *in vitro* against a number of filamentous fungi

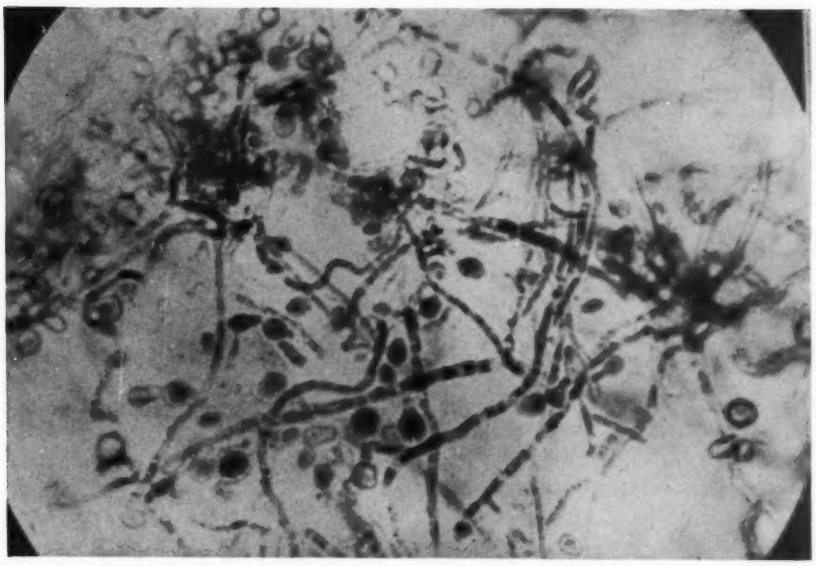


FIG. 4. Culture of blastomyces showing spherical or oval budding cells, fruit-bearing aerial hyphae and mycelium. (Courtesy of David T. Smith, M.D., Dept. of Bacteriology, Duke Univ. Medical School.)

but are less active against Monilia albicans. Although still in the experimental stage, these antifungal antibiotics have great possibilities as therapeutic agents.

TORULOSIS

Torulosis is caused by a yeast-like fungus, Torula histolytica, which reproduces only by budding without mycelial or endospore formation. Torulae are widely distributed in nature. They are found on trees, flowers, fruits, insects and grasses, and they have also been recovered from canned butter and canned milk. T. histolytica, when obtained from fresh material such as sputum, pus or spinal fluid and examined under the microscope unstained, may easily be mistaken for lymphocytes. They are ovoid or spherical cells, measuring 3 to 15 microns in diameter, and are enclosed by a definite cell wall which stains well with methylene blue.

A study of the reports of the recorded cases of systemic torulosis reveals that the infecting parasites have, primarily, a predilection for the tissues of the cerebrospinal system.[32] The symptoms resulting from the central nervous system invasion closely resemble the symptoms of tuberculous meningitis, intracranial neoplasm or abscess. The last two conditions are so realistically simulated that subtemporal and suboccipital decompressions have been erroneously performed in an effort to establish a diagnosis.[31]

Primary pulmonary torulosis is a rarity, and when found is usually an associated complication and secondary to cerebrospinal torulosis. In view of the fact that torulae are widely disseminated in nature, it has been suggested that the portal of entry is by way of the respiratory and digestive tracts.

Once the condition is diagnosed no time should be lost in instituting massive iodide therapy. Pulmonary resection has been reported as effecting a complete cure.[15]

BLASTOMYCOSIS

Blastomycosis, commonly known as Gilchrist's disease, is caused by a yeast-like fungus which appears in the lesion as an oval or spherical body, having a diameter of 10 to 20 microns consisting of finely granular protoplasm. It is enclosed in a double-contoured, highly refractive hyaline capsule. Multiplication in the tissues takes place by budding; however, some mycologists have reported reproduction by sporulation. On examination of cultures spherical or oval budding cells, fruit-bearing aerial hyphae and mycelium may be seen. (Fig. 4.)

Blastomycosis seems to attack people of the industrial classes chiefly, and males in a much larger proportion than females. The high incidence of infection in the male sex suggests that the natural reservoir of the fungus is in nature. Unfavorable hygienic surroundings, according

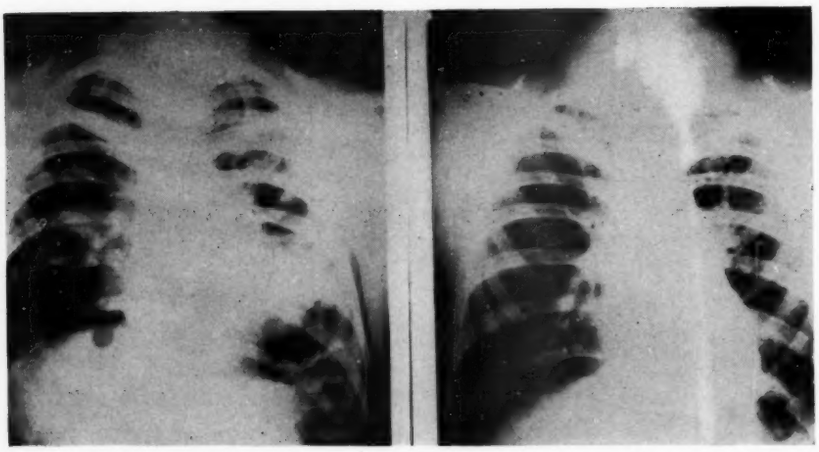


FIG. 5. Roentgenogram of patient with blastomycosis which responded to several weeks of intensive iodide therapy.

to Stober, seem to play a determinative role in its causation. Martin and Smith, in a recent complete study of the condition, state that although patients infected with this fungus have been found in all decades of life, no systemic infections have thus far been described in a patient under the age of twelve years or over the age of seventy.

Mode of Infection. Inhalation of contaminated dust or air probably plays the most important role in the transmission of the fungus deep into the respiratory tract. Recently a few cases have been reported in which there was a direct transmission of the disease from man to man. Evans reported a case of a pathologist who received a puncture wound on his finger while performing a necropsy on a patient with systemic blastomycosis. A primary infection developed at the site of the needle puncture and four months later blastomyces were demonstrated by biopsy and culture.

Mode of Onset. The cutaneous manifestations which are a characteristic feature of pulmonary blastomycosis may precede the onset of pulmonary symptoms. In their absence the condition is generally confused with that of tuberculosis. In a recent survey of the reported cases of pulmonary blastomycosis to date, nearly half have had no evidence of cutaneous lesions.

Pulmonary Involvement. Blastomycotic infection of the lungs constitutes the most frequent form of the systemic type of the disease. The clinical manifestations of the disease may have an acute or rapid onset, or the initial symptoms may resemble those of a cold or influenza and be so transient and mild as to escape the patient's attention. When acute in type the infection is usually ushered in with a chill, pain in the chest and symptoms of an acute respiratory infection which closely simulates the onset of lobar pneumonia.

Diagnosis and Treatment. The course of the disease is chronic with exacerbations and remissions. The symptoms and the clinical course of the disease closely resemble those of pyemia and advanced pulmonary tuberculosis.

The diagnosis can only be definitely established by the isolation and identification of the infecting organism. Frequently when the skin lesions are present, the diagnosis may be established by a recognition of the nature of the cutaneous lesions and the demonstration of the blastomyces in pus from the abscesses, or in a biopsy of the tissue. Early in the disease the roentgenograms, according to Potter,[16] usually show a dense irregular shadow extending from the hilum toward the periphery of the lung. In pulmonary infections of obscure etiology in which blastomycosis is suspected a skin test and complement fixation reaction should be performed.

Pulmonary blastomycosis is highly fatal, reaching a mortality much higher than that of tuberculosis. In an analytic study of 117 reported cases Martin and Smith[14] found that the mortality rate was 78 per cent.

The drugs of choice in the treatment of blastomycosis are stilbamidine[38] and potassium iodide. They may be used either alone or in a combined form of therapy. Stilbamidine is given intravenously in the dosage of 2 to

3 mg./kg. of body weight. The drug is dissolved in a solution of 5 per cent glucose in distilled water and administered by a slow intravenous drip. Schoenbach et al.[39] recommend that liver function tests and renal studies should be carried out before this form of therapy is instituted, since the drug may produce liver and renal damage when given over a long period of time. When iodides are employed, the course and method of treatment are similar to the one previously outlined for the treatment of moniliasis.

Martin and Smith recommend skin testing with standardized blastomyces vaccine before any form of therapy is considered. From their experience in the treatment of moniliasis they have also found that iodides are distinctly harmful if the patient is strongly allergic. Before instituting any form of iodide therapy in patients who show a marked allergic reaction, they recommend that an attempt be made to reduce the sensitivity by giving small desensitizing doses of vaccine. In recent years, due to the great progress made in the field of thoracic surgery, pulmonary resection has come to play an important part in the treatment of blastomycosis and other pulmonary fungous infections. In some clinics devoted to the diagnosis and treatment of pulmonary diseases iodides and vaccine therapy are first employed in the acute phase of blastomycosis in the hope of converting the disease to a chronic, well stabilized lesion which will be suitable for surgery. (Fig. 5.)

COCCIDIOIDAL GRANULOMA

Coccidioidal granuloma is a chronic infectious disease caused by the fungus Coccidioides immitis. It presents itself as a well defined disease of the skin or as a general infection involving both the skin and the internal organs. It is protean in its clinical manifestations and often presents a clinical picture closely resembling that of pulmonary tuberculosis and blastomycosis, both in symptoms and physical signs. The etiologic fungus, which morphologically closely resembles the blastomycete, appears in the tissues and in the pus from granulomatous lesions as an oval or spherical body, surrounded by a double-contoured hyaline capsule. The size varies from 5 to 50 microns in diameter. It differs from the blastomycete chiefly in multiplying in the tissues by sporulation, instead of by budding, although some mycologists have observed budding in fresh preparations of pus. (Figs. 6 to 8.)

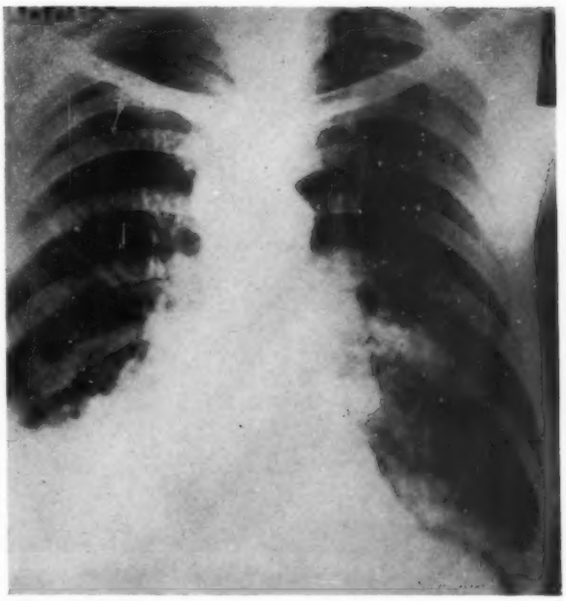


FIG. 6. Roentgenogram of patient with coccidioidal granuloma; case terminated fatally.

In a statistical study of the disease by far the largest number of reported cases have been from southern California and the San Joaquin Valley. Recently a small number of cases has been reported from other portions of the United States.[32] The condition was first described in this country by Rixford in 1895.[6] Persons of all ages and of either sex may be affected. The highest incidence of the disease appears to be in regions where there is prolonged hot, dry weather favorable to the dissemination of the spores. In 1936 the State Department of Health of California reported that since the initial case in 1895 a total of 450 cases with 224 deaths had occurred.

Trimble,[17] in an excellent review of the subject, calls attention to the fact that coccidioidomycosis should no longer be considered a rare disease confined to the southwestern part of the United States and certain parts of South America. It was shown that during World War II a high incidence of infection occurred in military personnel who were stationed in endemic areas. The author, located many miles from the southwestern part of the United States, has already seen a number of cases in his own community.

As in blastomycosis, cutaneous lesions may precede the onset of the pulmonary symp-

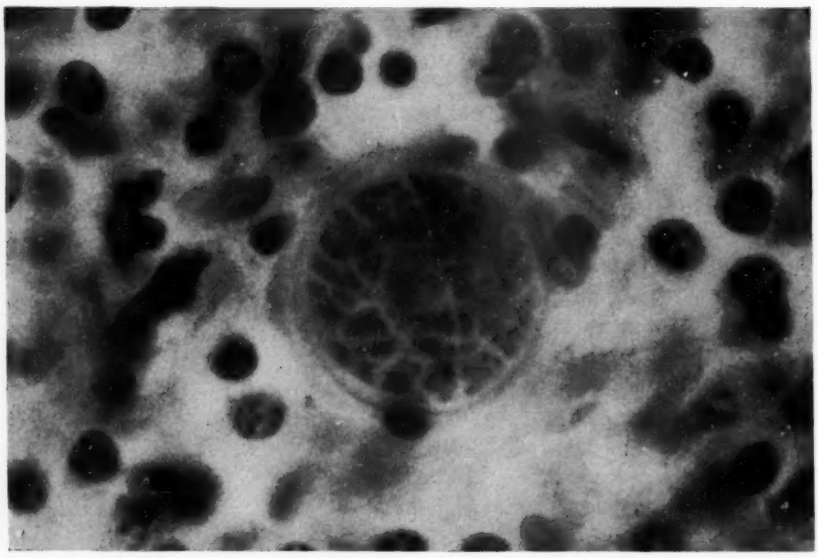


FIG. 7. Coccidioides in tissue section of lung, showing double-contoured hyaline capsule with formation of endospores.

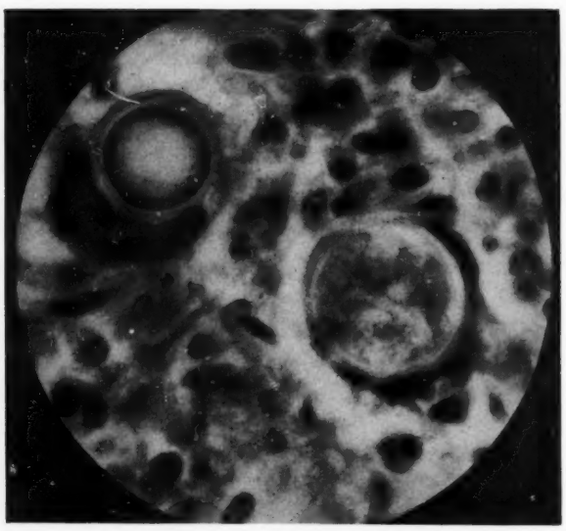


FIG. 8. Coccidioidal immitis in stained tissue preparation showing organisms containing typical endospores.

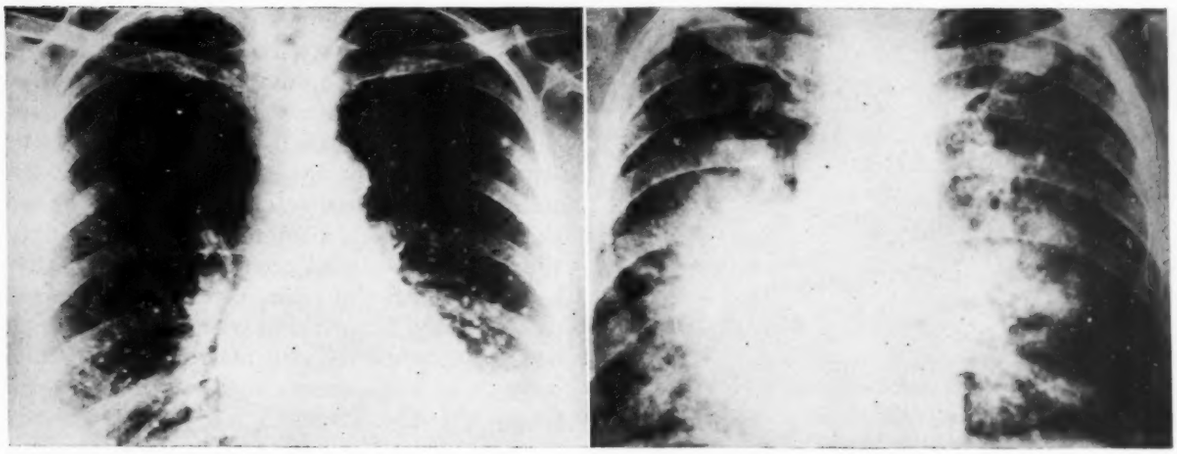
toms.[13] However, it is more common in coccidioidal granuloma to obtain a history of respiratory infection several weeks before the appearance of the external lesions. Dickson[18] described a condition called "valley fever" which is characterized by a cold or bronchopneumonia, often with a relatively high fever and the appearance of painful erythema nodosum. This, he stated, was the primary infection with coccidioides.

Trauma seems to be a predisposing factor and lesions often develop at the site of the traumatized area. Involvement of the epiphyseal ends of the long bones is very common in this condition. Many of the patients also develop large subcutaneous fluctuating abscesses from which pus can be aspirated with ease. In 1936, through the courtesy of Dr. Newton Evans, pathologist at the Los Angeles County Hospital, the author[13] had the good fortune to see several such cases in which many large, nodular, subcutaneous, fluctuating masses were present.

From a study of the roentgenograms of many of these cases Evans and Ball[19] make the following comment: "A diffuse shadow at times simulating pneumonia, occurs in many cases and involves the right lower lobe twice as frequently as any other part of the lung field, though it may occur in any portion, and twice as frequently in both hilar regions as in one. In many cases the lesions are those of a disseminated miliary tuberculosis."

Differential diagnosis of coccidioidal granuloma offers the following difficulty: (1) miliary bronchopneumonia; (2) miliary tuberculosis—acute or chronic; (3) carcinomatosis; (4) second stage silicosis; (5) other mycotic infections; (6) tuberculoma; (7) sarcoidosis; (8) hamartoma.

As in tuberculosis, it is believed that the primary focus of coccidioidal granuloma may remain dormant in the lungs for many years. In the acute coccidioidal infections some observers have estimated that the period of incubation is between two to three weeks.



9 10

FIG. 9. Benign form of histoplasmosis showing calcific deposits throughout both lung fields. Histoplasmin skin test and complement fixation were positive.

FIG. 10. Roentgenogram of patient with pulmonary histoplasmosis having a fatal termination.

The disseminated form carries a high mortality and all attempts in the medical treatment using various antifungal agents, such as prodigiosin, sodium caprylate, ethyl vanillate, stilbamidine and some of the newer aromatic diamidines, have proved unsatisfactory. In the skin form Ball has obtained encouraging results from the use of iodine in concentrated form. Tomlinson and Bancroft[20] expressed the opinion that the use of antimony and potassium tartrate, in addition to roentgen therapy, is of value. Jacobson[2] obtained fair results in a number of cases by intramuscular injections of colloidal copper combined with cutaneous injections of coccidioidin.

The most encouraging results to date in the treatment of the well defined granulomatous lesions with or without cavity formation has been brought about by pulmonary resection. In 1950 Cotton[17] reported a large series of cases in which he obtained excellent results by surgical intervention. Many of the patients on whom he operated had been under medical treatment for a long period of time and showed evidence of beginning cavity formation. Since pulmonary resection today has become such a relatively safe procedure, it should be employed more often in the treatment of this disease.

HISTOPLASMOSIS

In 1906 Darling, while working in Panama, first described the condition of histoplasmosis and isolated the causative fungus, Histoplasma capsulatum. The disease presents a variety of clinical and radiologic manifestations. Primary histoplasmosis occurs most often in the lungs, usually runs a benign course, and the resulting resolution of the filtrate generally leaves areas of multiple calcification in the parenchyma and regional lymph nodes. The progressive disseminated form of histoplasmosis carries a high mortality. In the fatal form of the disease the primary lesion is generally located in the mouth and upper respiratory tract. Primary pulmonary lesions are difficult to differentiate from a variety of acute and chronic infections of the lungs including acute respiratory disease, viral pneumonia, other mycotic infections and tuberculosis. (Figs. 9 and 10.)

The causative fungus, H. capsulatum, is a small, encapsulated, oval-shaped yeast-like fungus measuring 1 to 3 microns in diameter. It differs from all other fungi pathogenic for man in that the organism is primarily a parasite of the reticuloendothelial system. It is usually found in the mononuclear cells in peripheral blood smears, sternal bone marrow smears and in the cytoplasm of endothelial cells. The presence of the organism in sputum and gastric washings should stimulate further bacteriologic and serologic studies. Furcolow,[21] an outstanding authority on histoplasmosis, describes several serologic tests as aids in the diagnosis of this disease. Following a positive histoplasmin test he and his associates recommend the following procedures: (1) complement

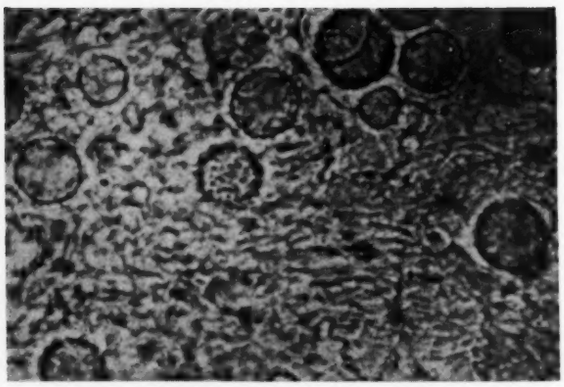


FIG. 11. Histoplasma capsulatum showing fungus with distinctive tuberculated border.

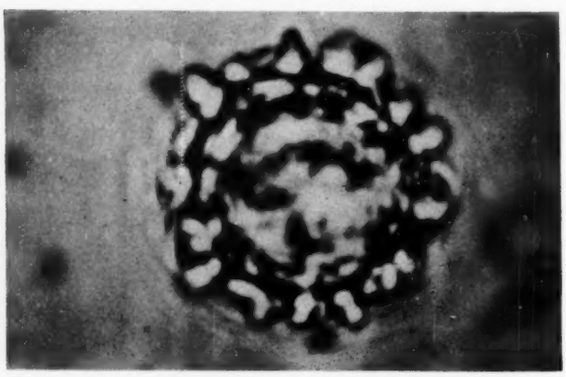


FIG. 12. Histoplasma capsulatum (magnified) showing a well defined tuberculated border. (Courtesy of Department of Medicine, Mayo Clinic.)

fixation, (2) collodion or red cell agglutination and (3) precipitin test. (Figs. 11 and 12.)

At the present time there is no specific therapy for the treatment of histoplasmosis. Fortunately, the great majority of patients with this disease recover without any form of special treatment. Christie and his associates[22] at Vanderbilt University have used ethyl vanillate with some encouraging results. Other investigators have found some value in the use of iodides combined with actidione therapy. In localized lesions pulmonary resection has produced a curative result.

SPOROTRICHOSIS

The pulmonary form is occasionally seen in this country, although by far the greatest number of cases have come from Europe. The largest number of reported cases in this country have occurred in the Mississippi River basin. The causative agent is a yeast-like fungus of either the Schenkii or Beurmanni type. It multiplies by budding, and in cultures it forms a mycelium composed of freely branching septate hyphae which in turn give rise to secondary conidia.

Infection may take place under various conditions and through a variety of agencies. Infected plant or vegetable matter carrying the organisms directly into an area of broken skin or mucous membrane probably constitute the most common source of infection. Foerster reported a series of cases in which the infection was acquired by pricking with the thorn of the barberry shrub. Certain insects, notably flies, wasps and ants, frequently carry and harbor the sporotricha parasites and the bite or sting of these insects may carry the organisms in the tissues and cause active infection.

The cutaneous lesions which develop in this condition are difficult to differentiate from the primary lesions of syphilis, cutaneous tuberculosis and the ulceroglandular type of tularemia. The fungi[13] of the Sporothrix group are very sensitive to the iodides and many of the reported cases have shown a complete cure following a short course of treatment. In the more resistant cutaneous lesions unfiltered x-ray radiations are used in combination with the iodides.

ASPERGILLOSIS

Pulmonary aspergillosis is commonly caused by a mold-like fungus, Aspergillus fumigatus, possessing a stem and a stalk with a spore-bearing head. Due to their resemblance to a brush this group of fungi derive their name from the word aspergillum, a brush which is used in the Catholic church for the sprinkling of holy water. (Figs. 13 to 15.)

There are three varieties of pathogenic Aspergillus—A. fumigatus, A. flavus and A. niger—which under conditions of lowered bronchial pulmonary resistance may cause an infection in the respiratory tract. The infection caused by these molds frequently runs a chronic course and the causative parasites seem to have a special affinity for the tissues of the pulmonary system. Occasionally the skin, sinuses and the external auditory canal are also involved. In this group of fungi there are also many non-pathogenic forms[33] which are used to good advantage commercially for the ripening of Roquefort cheese and the production of citric acid.

The first case of aspergillus infection in man was reported by Bennet in 1843.[23] Virchow[23]

first determined the identity of the parasites in 1856. Dieulafoy[25] reported the occurrence of aspergillosis among the pigeon feeders of France. Renon[26] described the same condition among the workers in the hair sorting industry and isolated A. fumigatus as the causative

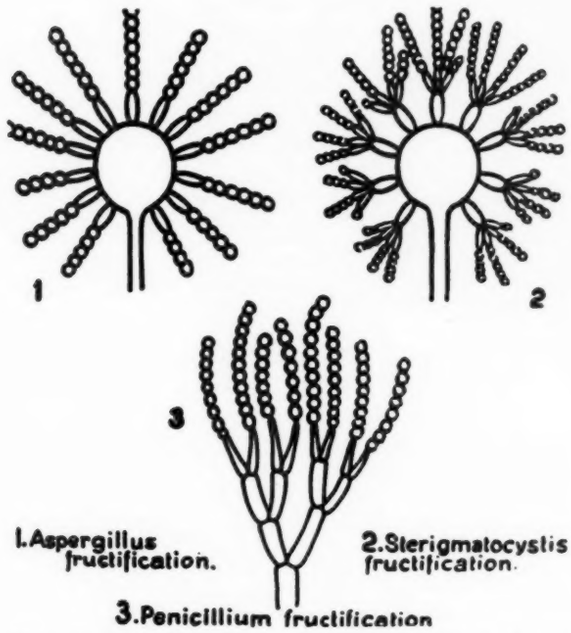


FIG. 13. Photograph of aspergilli showing stalk and spore-bearing head.

agent. In all of the previously reported cases the disease terminated fatally. In 1890 Widal[27] described clinically several cases of pulmonary aspergillosis occurring in persons who were engaged in fattening pigeons for the Paris market.

In 1926 Mary Lapham[28] reported ten cases of primary pulmonary aspergillosis from an obscure village in the Blue Ridge Mountains and divided the cases into two groups: the wet or parenchymatous type and the dry or interstitial type. She also called attention to a definite relationship to asthmatic attacks in certain cases.

Most pathologists describe the pulmonary form as falling into two characteristic groups: a superficial and a deep form. In the former are included cases of bronchitis, catarrhal or asthmatoid, which run a fairly benign form. The deep, or ulcerative type, depends upon the dosage and the ability of the endotoxins of the mold to cause necrosis of lung tissue analogous to the action of tuberculin in causing caseation in pulmonary tuberculosis. The asthmatic

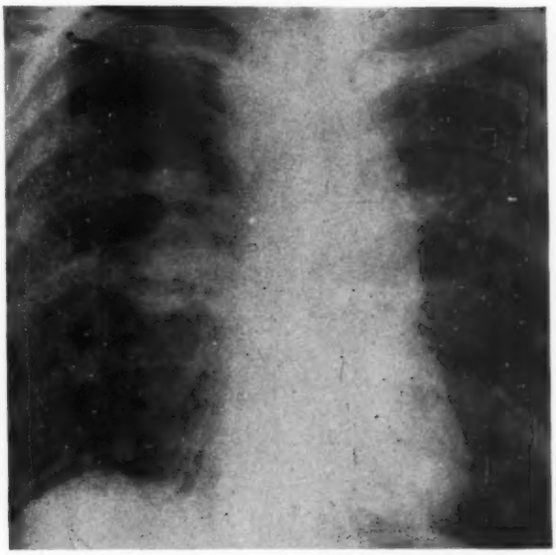


FIG. 14. Roentgenogram of patient with generalized pulmonary infection with A. fumigatus.

type of aspergillosis has resulted in the addition of a new chapter to the field of allergy. Allergists are well aware of the frequency of aspergillus sensitivity in asthma and allergic rhinitis. Today no allergic study is complete unless the skin testing for molds is performed.

Pulmonary aspergillosis, clinically and pathologically, so closely resembles pulmonary tuberculosis that it usually escapes recognition and is diagnosed as tuberculosis. The only roentgenologic findings which may be of diagnostic value is that in aspergillosis, migratory lobar and segmental atelectasis is commonly observed.

Hinson, Moon and Plummer,[29] in a recent and comprehensive review of the subject, call attention to the similarity of the radiologic findings with those seen in the so-called pulmonary eosinophilia (Loeffler's syndrome). They further call attention to the fact that in the eight cases which they recently reported a high blood eosinophilia was a constant finding.

Climatic, occupational and regional conditions may have some bearing on the development of this disease. In certain parts of the United States aspergillus infection does not seem to be of the severe pathogenic type. The majority of the cases having a fatal termination have been reported from Europe.

In the treatment of this condition particular attention must be paid to an existing allergic state. Various antifungal drugs previously

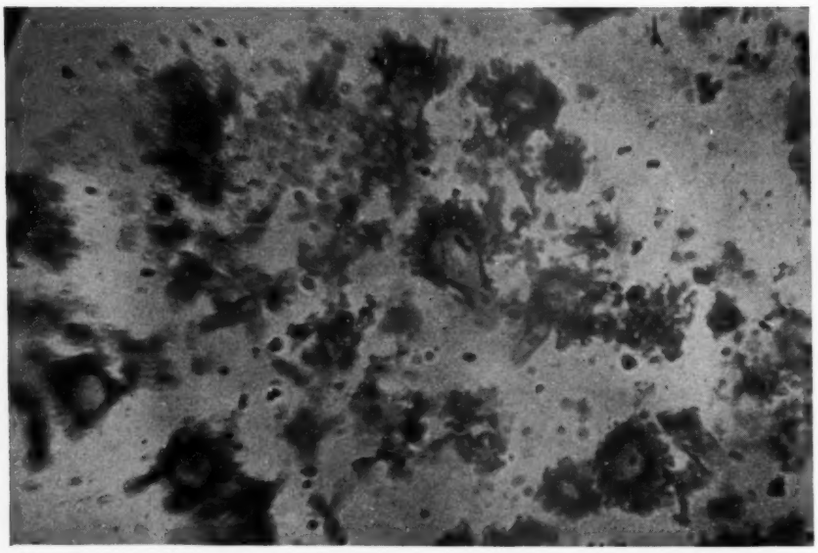


FIG. 15. Aspergillus, showing stalks and spore-bearing heads. The basal stems are not shown in this photograph. (Courtesy of Dr. N. S. Plummer, London.)

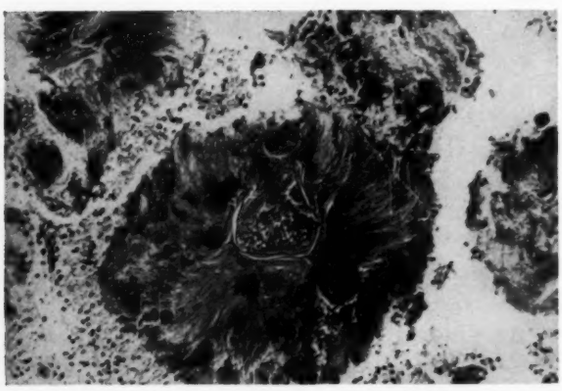


FIG. 16. Colony of ray fungus isolated from sputum bronchoscopically aspirated from patient with pulmonary actinomycosis. (Courtesy of Dr. C. B. Schoemperlen, Winnipeg, Canada.)

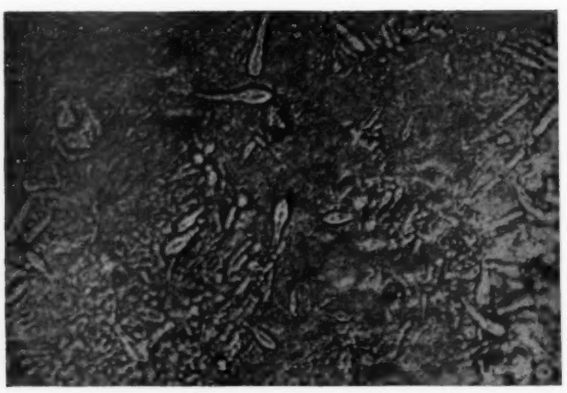


FIG. 17. Crushed actinomyces granule from fresh sputum unstained, under high-power magnification, showing the clubs or rays. In culture and stained preparations these are not seen.

described for the treatment of other mycosis, combined with ACTH and cortisone therapy, have produced encouraging results.

In localized lesions showing destructive pulmonary changes and complicated by bronchiectatic involvement, pulmonary resection is the choice of treatment.

ACTINOMYCOSIS

Bollinger first described this disease in cattle and showed that it was due to a vegetable parasite to which Harz,[24] because of its radiate structure, later gave the name of "Strahlenpilz" or Actinomyces. In 1878 Israel discovered the fungus in man, and later Ponfick pointed out the identity of the human and bovine infections. The first case of the disease to be recognized in this country was reported by Murphy in 1885. In 1923 Sanford[2] collected a total of 678 cases of actinomycosis from all the available sources in the United States and expressed the opinion that the number of cases represented only a small proportion of the actual number of victims suffering from this disease. Since Sanford's comprehensive study many more cases have been reported from all portions of the country.

Actinomycosis may be caused by any one of several species of fungi of the genus Nocardia, Actinomyces or Streptothrix.[11] The diagnosis of actinomycosis in any of its forms is ultimately dependent upon the finding of the

characteristic sulphur-like granules containing the ray fungus. This causative agent is present in the lesion and in the pus in the form of spherical or irregularly rounded grayish or yellow granules. When these so-called sulphur granules are crushed between slide and cover glass and examined with the microscope under high power, one sees an indefinite mass of tangled fibers and debris. Pus cells are found at the center, and at the periphery there is a dense network of interlacing filaments which at their extreme margin show the refractive club or rays. It is important that one sees both the rays and mycelium before establishing a definite diagnosis. (Figs. 16 and 17.)

Pulmonary actinomycosis is invariably fatal, and although this condition is often confused with tuberculosis, the clinical and pathologic course is quite different. There is no other pulmonary condition in which there is a tendency on the part of the disease to burrow its way in all directions. From a single lesion in the lungs one sees many sinuses radiating in all

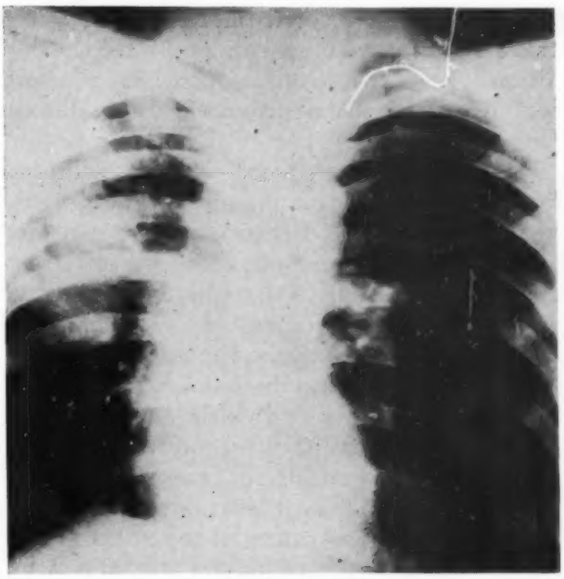


FIG. 18. Roentgenogram of thirty-five year old patient with pulmonary actinomycosis. This patient had been under observation for tuberculosis for several weeks. (Courtesy of Dr. C. B. Schoemperlen, Winnipeg, Canada.)

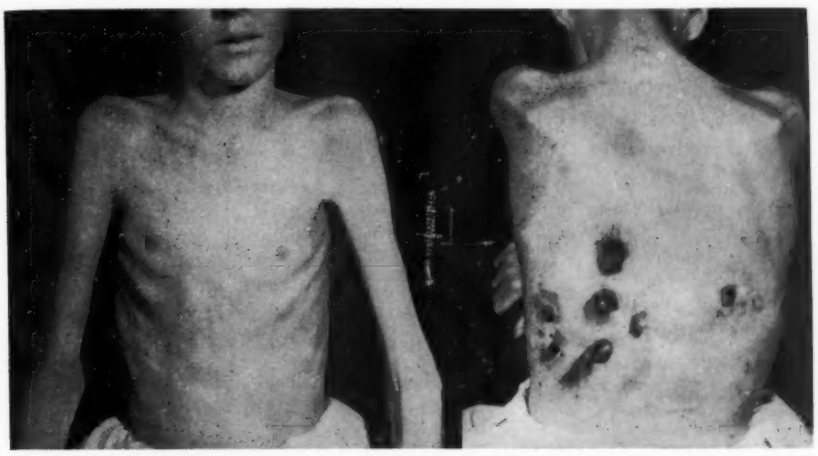


FIG. 19. The terminal or fistulous stage of actinomycosis so commonly seen not too long ago in many of our sanatoriums and general hospitals.

directions. The involvement of the neighboring organs by direct extension is a striking feature of this disease. Invasion of the pleura and peripleural tissues is almost invariable, and usually leads to the formation of adhesive pleurisy. Erosion of the ribs, perforation of the intercostal spaces in one or more places and superficial thoracic abscesses are often found. Invasion of the pericardium and the mediastinum with erosion of the vertebra takes place with regular frequency. (Fig. 18.)

Israel[26] has divided the clinical course of the disease into three stages. In the first, or bronchopulmonary, stage the process does not extend beyond the limits of the pulmonary tissue. Incidentally, it is in this stage that the condition might be amenable to surgery, for Actinomyces are usually anaerobic and with the entrance of air, which follows the free opening of the many sinus tracts and the resection of the circumscribed diseased tissue, a complete cure may be effected. Unfortunately, one almost never sees a patient in this early stage. Involvement of the pleura marks the beginning of the second, or pleurothoracic, stage while invasion of the thoracic wall termi-

nates in the third, or fistulous, stage. It is in this stage that we most commonly see the condition. This classification presents a useful picture of the usual progress of the disease. (Fig. 19.)

The medical treatment of this condition makes up one of the gloomy chapters in the history of medicine. Because of the seriousness of the condition numerous attempts have been made to discover some therapeutic agent which would arrest the progress of the disease and alleviate the sufferings of the patient. As yet, however, nothing specific has been discovered to accomplish this end with any degree of certainty. In 1937 Myers reported successful treatment in five of his six cases of actinomycosis affecting different portions of the body by the oral administration of thymol. Employing Myers' method, in 1939 Etter and Schumacher[30] reported a case of pulmonary actinomycosis successfully treated by thymol. Their patient received 30 gr. of thymol daily for a period of seventeen days. Other investigators have reported successful treatment by the use of massive doses of potassium iodide. Because of the numerous respiratory infections responding to the sulfonamides and antibiotic therapy these agents have been used in combination with iodides. Bevan[2] advocates the use of copper sulphate in ¼ gr. doses several times daily. Non-specific protein therapy has been successfully employed by Epstein in two cases of actinomycosis.

The only satisfactory method in dealing with the accessible type of this disease is radical surgery. In view of the rapid progress being made today in the field of thoracic surgery, there is great hope that the pulmonary form of this disease may be successfully treated by the thoracic surgeon.

SUMMARY AND CONCLUSIONS

In this brief review of the mycotic infections of the lungs the author has attempted to emphasize the following:

1. The close resemblance between this type of infection and that of pulmonary tuberculosis.

2. Pneumomycotic infections undoubtedly occur more often than is generally suspected or recognized, and in obscure pulmonary infections the possibility of this condition should always be considered.

3. The importance of the laboratory as an indispensable means of establishing the early diagnosis.

4. Once the diagnosis has been definitely established, antifungal therapy, as previously outlined, should immediately be instituted. In suitable cases pulmonary resection may effect a complete cure.

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Whether a thymoma is present or not, about one-third of the cases of myasthenia gravis will be greatly improved by thymectomy, and perhaps never again require prostigmin.® Another third of the cases will be greatly improved after thymectomy but will still require therapy with prostigmin. In about 10 per cent thymectomy is of no apparent value in the therapy of myasthenia gravis. (*Richard A. Leonardo, M.D.*)

Pulmonary Histoplasmosis

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HISTOPLASMOSIS is a highly infectious mycosis caused by Histoplasma capsulatum and presents a variety of clinical, pathologic and roentgenologic manifestations. Although first described by Darling in Panama in 1906[1] as a protozoon, the organism was later shown to be a fungus[2] and was placed in the Fungi Imperfecti by Conant in 1941.[3] Skin testing surveys have shown the disease to be highly endemic in the Mississippi and Ohio Valleys and along the Appalachian mountains. In certain local areas sensitivity to intradermal histoplasmin may be as high as 80 per cent of the adult population. Fringe areas of lesser sensitivity extend outward from these regions.[4]

It is now well established that the usual route of infection is the respiratory passage giving rise to a primary focus or primary foci within the lungs. The extensive studies of Christie and Peterson,[5] and Furculow and his associates[6] have shown that most histoplasmoses exist in the form of a relatively benign primary pulmonary infection. Primary histoplasmosis is clinically indistinguishable from common upper respiratory infections and may be asymptomatic. It usually has a short benign course and healing may result in complete resolution. More frequently healing leaves one to many discrete, scattered, fibrotic or more often calcified lesions in one or more lobes. In a small percentage of cases the primary form is progressive resulting in disseminated histoplasmosis usually characterized by involvement of all organs of the body. Disseminated histoplasmosis is usually fatal and has been shown to occur more frequently at both extremes of the life span.[7] The disseminated form has been covered in a number of excellent reviews.[7–10]

One characteristic of histoplasmosis is its tendency to occur in epidemics following exposure in heavily contaminated areas by groups of persons. Epidemic histoplasmosis is characterized by widespread involvement of the lungs, a severe and frequently prolonged illness but is rarely fatal. Grayston and Furcolow[11] have recently studied thirteen epidemics and called attention to the frequency of disseminated pulmonary calcification following recovery. Loosli and his associates published an extensive three-year follow-up of a small epidemic in one family.[12]

There is increasing evidence that a chronic active form of pulmonary histoplasmosis exists that closely mimics pulmonary tuberculosis. Some of these cases may be reinfection histoplasmosis. As an example Johnson and Batson's case contained an apical cavity, fibrotic infiltrations in the contralateral apex, and scattered calcified lesions in the remainder of the lung fields.[13] Sutliff and his associates[14] reviewed eleven cases of chronic pulmonary histoplasmosis, called attention to the location frequently being in the upper lobes and mentioned that the process was usually fibrocavitary. It is apparent that this form of the disease is intermediate between uncomplicated primary histoplasmosis and widely disseminated histoplasmosis in its course. It is also this form that appears to be amenable to definitive surgical therapy.[10,15,16]

OBSERVATIONS

The present series consists of sixty-seven cases from which pulmonary tissue, hilar nodes, or both were removed and H. capsulatum was identified in the resected material. It is emphasized that in all cases the disease process is believed to have been stabilized. The cases are therefore probably best classified as healed or healing primary histoplasmosis. Thirty of these cases have been previously reported.[17,18] Nine patients were white women and fifty-eight were white men. In all cases there was a history of residence in known endemic areas for periods of from one to twenty years. Table 1 shows the patients by age group.

Almost one-half of the patients were in the age group twenty-one to thirty years. It should be borne in mind that patients in the

Army are predominantly young males. As already mentioned disseminated histoplasmosis is more common at both extremes of the normal life span. During the intermediate period of life more cases seem to occur in young adult males, probably due to more frequent exposure. A similar predominance in adult males has been noted in other fungous diseases.[19,20]

TABLE 1
AGE GROUPS FOR SIXTY-SEVEN PATIENTS WITH PULMONARY HISTOPLASMOSIS

Age (yr.)	No. of Cases
18 to 20	4
21 to 30	31
31 to 40	22
41 to 50	8
51 to 60	1
61 to 70	1

The preoperative diagnoses varied greatly. Many of the cases were referred to Fitzsimons Army Hospital with a diagnosis of "tuberculoma" and others as "coin lesion" of the lung. A presumptive diagnosis of histoplasmosis was made in several cases that were asymptomatic; were positive reactors to intradermal histoplasmin and negative reactors to intradermal coccidioidin and tuberculin. Focalized coccidioidomycosis was considered in those patients with residence in endemic areas. Some patients showing multiple nodose lesions by roentgenograms and having a positive reaction to tuberculin were given a presumptive diagnosis of tuberculosis and a few underwent trial courses of chemotherapy for tuberculosis without change in the roentgenograms. The diagnoses of lymphoma or sarcoid were considered in several cases showing only hilar node enlargement. One patient showing a cavity was thought to have tuberculosis as a positive reaction to both histoplasmin and tuberculin was present. The diagnosis of neoplasm was entertained in several patients in the older age groups. In one case the pulmonary lesion was thought to be metastatic since the patient had had a malignant tumor elsewhere. In no instance could the presumptive diagnosis of histoplasmosis be confirmed by cultural methods preoperatively.

SYMPTOMATOLOGY

Thirty-one patients in this series were completely asymptomatic and the lesions were found by routine chest roentgenograms taken for reenlistment, annual physical examinations or, in three cases, in connection with investigation of complaints other than those referable to the pulmonary system. Eight patients complained of malaise, easy fatigue and weight loss varying from 10 to 25 pounds over periods up to two years. Eight patients had blood-streaked sputum on one or more occasions. One patient had two bouts of frank hemoptysis. Eight patients had fever (the highest 103°F.) and all fevers were associated with symptoms referable to the upper respiratory tract. Ten patients complained of transient pleural pain. Fifteen patients estimated their onset to coincide with a rather mild but prolonged upper respiratory infection. Five cases presented the typical symptoms and clinical findings of a middle lobe syndrome.[21] Three of these cases are being reported in detail elsewhere.[22]

In four cases the lesions were considered incidental findings in pulmonary tissue removed for the therapy of other conditions. One patient had proven tuberculosis with lesions in both the right upper and right lower lobes. Under prolonged chemotherapy the upper lobe lesions regressed but residuals remained. The lower lobe lesion did not change. Thoracotomy was performed and residual lesions from both lobes were removed. The lower lobe lesion was found to be histoplasmosis with no tuberculosis in the segment of lung removed. The upper lobe contained caseonodose tuberculosis. In one case the left lower lobe was removed because of bronchiectasis. Five discrete 0.3 to 0.5 cm. nodules containing H. capsulatum were present deep in the lung parenchyma. The third case, a twenty-nine year old white man, had a left upper lobectomy for palliative treatment of bronchogenic carcinoma. This patient gave a history of a spontaneous pneumothorax and large emphysematous blebs were present in the apex. An 0.5 cm. isolated lesion containing H. capsulatum was present adjacent to the tumor. Another patient gave a history of spontaneous pneumothorax on three previous occasions. Wedge resection of apical emphysematous blebs was performed and a 1.0 cm. partially calcified nodule containing H. capsulatum was present in the subpleural region. It is not believed that histoplasmosis contributed to spontaneous pneumothorax in the latter two cases.

Physical examination was non-contributory

or gave non-specific information as would be expected in stabilized lesions of the type removed. In one case there was pleural effusion following pleural pain with slight dyspnea. Thoracentesis on five occasions over a period of two years yielded up to 500 cc.'s of sterile fluid with cell counts up to 1,400 per cu. mm., with 95 per cent polymorphonuclear cells. Decortication of pleura and wedge resection of pulmonary tissue containing a granuloma due to H. capsulatum were performed. This patient had a positive tuberculin test and one cannot be certain that his effusion was due to histoplasmosis. No other case in this series was known to have had pleural effusion.

LABORATORY DATA

Routine examinations of the blood and urine were performed on all patients. There were no significant deviations from normal. Increased sedimentation rates were noted at some time in fourteen of the cases. The highest was 43 mm. per hour (Wintrobe).

Bacteriology. Attempts to culture the organism from resected material in the present series have given disappointing results. In contrast to other fungi H. capsulatum is known to be fastidious in its growth habits and various investigators have reported difficulty in culturing the organism and in reproducing the disease in animals.[23,24] On the other hand Ajello and Runyon[25] were able to infect mice with a single spore and there seems to be little difficulty in isolating the organism from disseminated or active primary cases when fresh sputum is used as suggested by Kurung.[26] Almost all patients in the present series had preoperative cultures of sputum and gastric washings for fungi and acid-fast bacilli, all with negative results. Three methods of culturing material from resected specimens were tried. Originally, scrapings from the cut surface of granulomas were emulsified and the material inoculated on culture plates. Later generous portions of resected tissue from each patient were ground, emulsified and plates inoculated. Finally, on the advice of Furcolow,[27] material from the lesions was ground and emulsions were injected intraperitoneally into several mice. After fourteen days, one group of animals was sacrificed, their livers and spleens were emulsified and this material was inoculated on culture plates. After sixty days the remaining animals were sacrificed and similar cultures made. All specimens were cultured on B.H.I.* blood agar with streptomycin and penicillin added after the method of Howell.[23] Duplicate plates were inoculated, one group incubated at room temperature, one at 37°C. In addition other standard media were occasionally used.

TABLE II
RESULTS OF INTRACUTANEOUS HISTOPLASMIN, COCCIDIOIDIN AND TUBERCULIN IN SIXTY-THREE CASES

Histoplasmin	Coccidioidin	P.P.D.		No. of Cases
		0.00002 mg.	0.005 mg.	
+	+	−	+	3
+	+	−	−	4
+	+	+	..	8
+	−	−	+	11
+	−	+	..	16
+	−	−	−	20
−	−	−	+	1

Note: +, positive reaction; −, negative reaction.

Specimens were also cultured for acid-fast bacilli using Petragnani's medium. The only cultures positive for H. capsulatum were those from a cavitary lesion and from a parenchymal lesion in a case presenting a middle lobe syndrome. All cultures for acid-fast bacilli were negative. Tissue sections stained by the periodic acid-Schiff (PAS) stain[28] were positive for H. capsulatum in all cases. Direct smears and tissue stains for acid-fast bacilli were negative in all cases.

Cutaneous Reaction. Table II shows the results of intracutaneous histoplasmin, coccidioidin and tuberculin in the sixty-three cases that were tested.

There is much controversy over the value of the intradermal histoplasmin test to other than the epidemiologist. It is known that as many as 50 per cent of the disseminated cases may give a negative reaction[10] when in the terminal phase. It has been established that a high percentage of cases of disseminated coccidioidomycosis may not react to intradermal coccidioidin. It is well known that overwhelming tuberculosis may result in anergy to tuberculin. In the disseminated fungus diseases and in overwhelming tuberculosis the diagnosis is rarely a problem and may be readily con-

* Brain-heart infusion.

firmed by direct smears and cultures of appropriate material. It is in the focalized lesion that the intradermal tests are most valuable and help to guide the thinking of both clinician and pathologist. In the present series one patient did not react to histoplasmin. Unfortunately we were unable to repeat this test after organisms were found in the lesion. Obviously if patients react to two or more antigens, the information gained is of less value to the clinician. In a significant number of cases, however, (twenty in this series) patients react only to histoplasmin and the information obtained is of material value in evaluating the lesion. Intradermal coccidioidin in the *usual strength* is less reliable however,[29] and negative reactions do not rule out inactive focalized coccidioidomycosis.

Serologic Studies. Complement fixation tests and collodion agglutination tests were performed by the Army Medical Service Graduate School on thirty patients. The complement fixation test was negative in fifteen cases; was positive at 1:5 dilution in five cases; 1:10 dilution in five cases; 1:20 dilution in two cases; 1:40 dilution in two cases and 1:64 dilution in one case. The collodion agglutination test was negative in twenty-three cases; positive at 1:10 in three cases; 1:20 in three cases; and positive at 1:40 in one case.

Like other laboratory tests the serologic tests for histoplasmosis are of most value to those that have studied and understand their pitfalls and limitations. At the present time new antigens are being developed and the problem of cross reaction with other antibodies is being studied. A precipitin test has been developed that shows promise for use in early acute primary histoplasmosis, an area where the complement fixation test has been of little value.[30] Nevertheless, there are some generalizations that can be made on the basis of present information and some patterns that are fairly consistent and useful for diagnosis and prognosis.[31] In acute primary self-limiting histoplasmosis the complement fixing antibody appears early with a peak titer of 1:80 to 1:2560 within six weeks of the onset. These titers remain for only a short time and by the fourth month the titer is usually 1:20 or less. In chronic histoplasmosis the titer remains higher (1:160 or more) and clinical improvement is accompanied by a gradual fall. In advanced generalized histoplasmosis the titers are low or antibodies are not demonstrable. Cutaneous or mucocutaneous histoplasmosis has low titer or no titer as determined by the complement fixation test. Cross reaction with an antigen from Coccidioides immitis is rare; if present is of low titer (1:20 or less) and is accompanied by much higher homologous levels. Sera from all types of histoplasmosis will react with antigens of Blastomyces dermatitidis, however. Cross reactions in the collodion agglutination test in which histoplasmin is used as an antigen, are more extensive and positive results from this test can only be interpreted as presumptive evidence of a mycotic infection. The results of serologic studies of the present series are consistent with the inactive or healing lesions that were found to be present.

PATHOLOGY

The intralobar location of the lesions in the sixty-four cases studied were as follows: right upper lobe, twelve; right middle lobe, fourteen; right lower lobe, eleven; left upper lobe, twelve; and left lower lobe, seventeen. Two cases in which lesions were removed from two different lobes are included.

Thoracic Cavity. Hilar or mediastinal nodes only were removed in three cases. Masses of nodes varied from 1.0 cm. to 2.5 cm. in diameter, were firm and rubbery. All contained large conglomerate foci of necrotic material in which organisms could be found. In four patients presenting the middle lobe syndrome, the nodes about the hilum were enlarged (Fig. 1) and contained necrotic foci; their enlargement compressed bronchi giving rise to symptoms of obstruction. A fifth patient also had enlarged nodes compressing the middle lobe bronchus but in addition there were focal partially hyalinized necrotic lesions within the adjacent pulmonary tissue. In the latter case hilar nodes were calcified, had ulcerated the bronchial mucosa and fragments of calcified material were extruding into the lumen of the bronchus. Slightly enlarged hilar nodes were removed with parenchymal lesions in an additional three cases. These nodes also contained necrotic foci in which organisms were found. In addition, small discrete, firm hilar nodes were described by the surgeon in eleven cases from which parenchymal lesions were removed. It is our belief that these hilar nodes represent the central component of a primary complex analogous to that seen in

FIG. 1. Histoplasmosis, hilar node resulting in middle lobe syndrome; note compression of bronchus.

tuberculosis and coccidioidomycosis. In the present series it would appear that the central component is ordinarily small. In forty-eight cases hilar and mediastinal nodes were described by the surgeon as normal (thirty-five cases) or were not mentioned in the operative report (thirteen cases). The experience of Schulz[32] has been that the central component of the complex is frequently large. He believes that this discrepancy is best explained by the fact that his cases were in infants which may represent a true primary infection resembling tuberculosis, while adults with localized lesions may represent reinfection disease. Another factor to be considered is the duration of the disease. In Schulz's cases the disease was of only a few months' duration. In the present series the onset could not be determined with accuracy in many cases but a review of previous roentgenograms, the presence of calcium in some lesions, and the histology of the lesions leads one to believe that most lesions were of more than one year's duration at the time of removal. It is probable that with stabilization and resolution of perifocal reaction the involved lymph nodes may decrease in size.

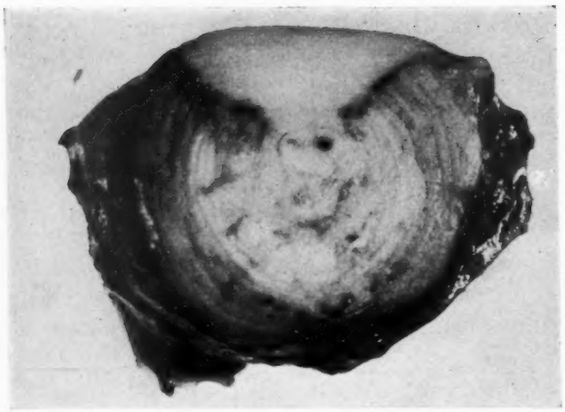

FIG. 2. Histoplasmosis; note pleural plaque, keystone, laminated appearance and central necrotic focus.

In the one case with a history of pleural effusion there was fusion of visceral and parietal pleura necessitating decortication. Microscopic examination of the pleura removed showed a chronic non-specific fibrous pleuritis with no granulomas, epithelioid reaction or necrotic foci, and no organisms could be found. As already mentioned the effusion was sterile. One cannot therefore be certain that the effusion and pleuritis were due to histoplasmosis. In six other cases fibrous adhesions to the parietal pleura or across interlobar septa were described. Adhesions were small, usually apical, were associated with pulmonary disorder other than histoplasmosis or were present in patients reacting to intradermal tuberculin. In no instance were there adhesions between parietal pleura and thickened visceral pleura over parenchymal lesions containing H. capsulatum.

Gross Appearance of Lesions. The parenchymal lesion or lesions removed varied from 0.5 cm. to 3.5 cm. in diameter. They were usually round, occasionally ovoid and their consistency varied from stony hard to firm and rubbery. The majority were located in the immediate subpleural region and approximately one-half were associated with a round, oval or stellate pleural plaque that was fused to the more peripheral portion of the lesion. The color of the plaque varied from a pearly pinkish gray to a light yellowish tan probably according to the age of the lesion. Infrequently there were 0.1 cm. nodules within the pleura a short distance from the main plaque representing spread by pleural lymphatics.

Usually the pleural plaque extended into the main mass of the lesion to form a keystone. In the older lesions there was a tendency for

the cut surface to show a concentric laminated appearance with deposits of pigment at the interfaces between the laminations. (Fig. 2.) In the younger lesions the cut surface was of a more homogeneous appearance. Without exception there was a small focus, usually central, that presented a softer appearance than the remainder of the lesion. Often this focus contained soft, granular, necrotic material; in other cases it was soft but rubbery.

Approximately one-half of the cases consisted of a single isolated sharply demarcated lesion such as that already described. (Fig. 3.) Frequently there were one or more satellite lesions that varied from 0.2 cm. in diameter to a size almost equal to the main lesion. Occasionally there were multiple nodose discrete lesions with smaller lesions present in the pleura and along vessels and bronchioles, probably representing lymphatic spread from the original lesions. Where multiple lesions were present, they all appeared to be of the same age.

In one case the lesion was a 2.0 by 3.0 cm. cavity from the left apex. The pleura was thickened and puckered over the cavity and no gross bronchial communication could be demonstrated. The cavity was lined by soft friable necrotic material and the adjacent pulmonary tissue was firm, had a granular cut surface with prominence of the small bronchi and vessels.

Microscopic Appearance. The microscopic appearance of the lesions was quite uniform. The larger lesions appeared to represent encapsulated foci of coagulative pneumonia in which alveolar outlines could be readily discerned except in the central necrotic portion. The latter area was usually made up of amorphous material and calcification, if present, appeared to have started in the periphery of this focus. In a few cases there was not a loss of alveolar outlines in the central necrotic focus but the material contained within the ghost outlines took the green counterstain of the PAS stain more intensely than elsewhere in the lesion. Lesions with this configuration had no central calcification. Organisms were always found in or immediately adjacent to these central areas, never around the peripheral portion where fibrosis was marked nor were they scattered diffusely through the entire lesion.

The peripheral portions of the larger foci were made up of dense fibrous tissue usually enclosing a thin zone of epithelioid cells. There was usually a slight to moderate lymphocytic infiltration around the periphery. Occasionally small bronchioles could be seen entering the peripheral fibrotic areas and in two cases cartilage could be seen incorporated within the fibrous tissue indicating previous communication with a larger bronchus.

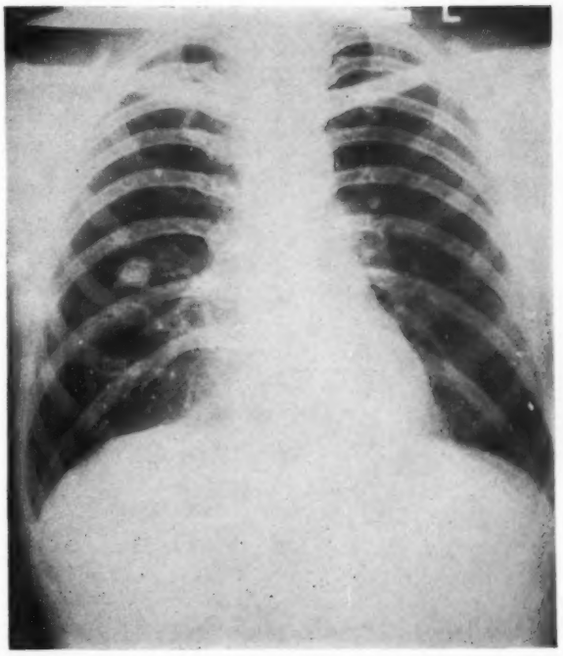

FIG. 3. Roentgenogram of focalized histoplasmosis; typical of the coin lesion seen in many cases.

The wall of the cavitary lesion was made up of dense fibrous tissue lined by necrotic material and cellular debris. A small bronchus was seen to enter the cavity and there was a patent bronchocavitary junction. There was squamous metaplasia of the bronchial epithelium and it extended into the cavity to line the lumen for a short distance giving way to the necrotic material that lined the remainder of the cavity. Organisms were scarce but were present in giant cells and mononuclear cells embedded in the necrotic material.

The reaction within adjacent pulmonary tissue varied somewhat, probably with the age of the lesion. In many cases there was no reaction other than thickening of alveolar walls in contact with the fibrous portion of the lesion. Other cases, notably those with adjacent satellite lesions, showed small foci of organized pneumonia, thickening of interlobular septa, vascular thickening and endarteritis, and non-

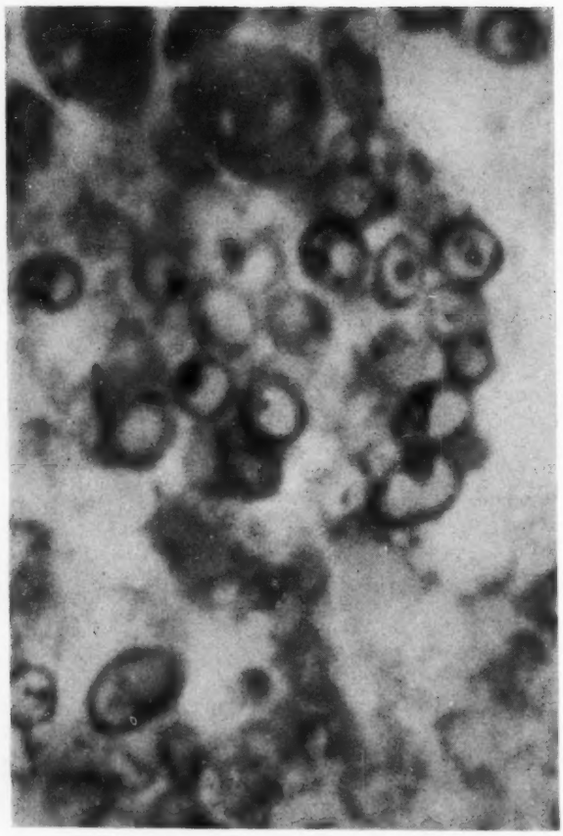

FIG. 4. Histoplasma capsulatum in necrotic focus (PAS stain).

specific bronchitis and peribronchiolitis. The most marked reaction was in the case containing a cavity in which there was a granulomatous pneumonia with lobular distribution. In other cases there were small epithelioid tubercles as well as hyalinized scars representing healed necrotic foci. Organisms were not found outside of the encapsulated foci or outside of the cavity, nor were they found in the small epithelioid tubercles showing no necrosis. There was no suggestion that the larger lesions were formed by conglomeration of smaller foci. In some cases small lesions were fused but did not break down at the point of fusion.

The lesions within lymph nodes were also quite uniform. In general almost the entire nodal architecture was replaced by a granular amorphous necrotic mass that was irregular and appeared to have been formed by conglomeration of adjacent foci. In some cases there were thin zones of fibrous tissue surrounding these lesions. Organisms were present in small aggregates, clusters or scattered singly in no constant region within the necrotic areas.

The pleura overlying the parenchymal lesions showed dense fibrous thickening with little or no inflammatory reaction. Occasionally there were encapsulated necrotic lesions containing organisms within the pleura. More frequently there were round hyalinized scars in which no organisms could be identified.

COMMENTS

In the past there has been a tendency on the part of some surgeons as well as pathologists to consider all isolated subpleural granulomatous lesions as "tuberculomas." This was based upon gross and microscopic appearance but in the absence of demonstrable tubercle bacilli. It has been known since Cox and Smith's paper in 1939[33] that coccidioidomycosis may leave a residual lesion grossly indistinguishable from the so-called "tuberculoma." The present writer has shown that histoplasmosis may leave residual lesions that are grossly indistinguishable from either of the above lesions.[17] More recently Zimmerman[34] has studied a group of thirty-five so-called "tuberculomas" from the files of the Armed Forces Institute of Pathology. He was able to find H. capsulatum in nineteen cases, C. immitis in three cases, Mycobacterium tuberculosis in six cases and no organism in seven cases. It is pertinent to re-emphasize that except for the presence of the offending organisms there are no clear-cut gross or microscopic characteristics by which isolated granulomas due to histoplasmosis, coccidioidomycosis or tuberculosis may be separated. It might be added that since we have adopted the periodic acid-Schiff stain as a routine procedure in the study of pulmonary granulomas we have come to regard the classic tuberculoma as an uncommon lesion.

The present writer has emphasized the difficulties in identifying H. capsulatum in focalized lesions.[17] The study of additional cases has shown the need for further emphasis. Organisms cannot be identified in necrotic foci when sections are stained with hematoxylin and eosin as used for routine stains. In our experience the periodic acid-Schiff stain as modified by Kligman and Mescon[28] has proved to be a most satisfactory procedure because it preserves the morphology of the organism. (Fig. 4.) Unfortunately, it is not specific for cytoplasm and it is therefore frequently necessary to use the oil immersion lens for confirmation as concretions, cellular inclusions and other

artifacts may simulate H. capsulatum. Frequently there are only one or two areas within a single granuloma in which organisms may be found. It is, therefore, advisable to use care in preparing sections and in many cases to section all material remaining after cultures are taken.

Classically, H. capsulatum has been described as an intracellular inhabitant and most descriptions state that it is infrequently found extracellularly. That is not the case with organisms found in the central necrotic portions of granulomas. In the latter regions they may be found in clusters, in pairs and scattered singly with only an occasional ghost of a cell outline about them. In the older lesions the organisms may assume a somewhat atypical morphology in that there may be more than the usual number of elongated and distorted forms, the central mass may be smaller and the limiting membrane thinner than in organisms seen with active disease. The present writer believes that these characteristics are manifestations of degeneration and that the organisms are probably not viable. This concept is supported by our difficulty in culturing organisms from these older lesions that are histologically stabilized.

There have been no known recurrences or postoperative spread of histoplasmosis in the patients from this series. The postoperative follow-up has been three years in ten patients and slightly over two years in fifteen patients.

SUMMARY

Pulmonary histoplasmosis is a common disease entity that achieves surgical importance mainly because of its propensity to leave residual foci that mimic tuberculosis, neoplasms or other diseases.

It is believed that organisms in these stabilized residual foci in most instances are nonviable. They commonly show atypical morphology and attempts to culture them from resected lesions has been disappointing.

It is emphasized that special staining procedures and meticulous care in examination should be given all granulomatous lesions. A complete history and the response to intradermal antigens should be known at the time the tissue is examined.

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Surgical Considerations in Pulmonary Coccidioidomycosis

REPORT OF 100 CASES

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COMPLICATIONS of pulmonary coccidioidomycosis present a problem of national interest, for the disease is now widely spread in our population. During World War II the Armed Forces had to place millions of troops in the endemic areas of the United States. Fully 25 per cent of reported infections occurred at that time among military personnel.[1] Residual complications among veterans are so widespread that most of the Veterans Administration hospitals have written papers on the problems of coccidioidomycosis—complicated, uncomplicated and with coexisting disease. In addition, many installations in endemic areas were reopened during the Korean conflict.

Other factors besides the military have contributed to the increase. Rapid postwar expansion of population in Los Angeles County, a region of minor endemicity, has resulted in a corresponding expansion of population in the nearby San Joaquin Valley whose soil has the world's highest concentration of Coccidioides immitis. Today over the Valley's four-lane highways there is a continual populous movement of business personnel, truckers, vacationers and migratory laborers.

Southern portions of those Southwestern states which border on Mexico are endemic areas, and in nearly all of these there have been similar expansions in population. As a result of all these population shifts and of increased transportation facilities, the disease may today be seen anywhere in the United States, or, for that matter, anywhere in the world.[1]

An idea of the increase in coccidioidomycosis is furnished by the fact that from 1892 (the year Wernicke first reported the disease) until 1936 there were only 400 odd cases reported in the entire world literature.[2] On the other hand, one of us (J. W. B.) has reviewed 750 cases of coccidioidomycosis, and nearly all of them were seen within the past decade in Kern County, California.

Complications of pulmonary coccidioidomycosis which may occur as sequelae of the acute infection were stressed by us in a previous publication.[3] These complications are: (1) extreme hilar adenopathy, (2) coccidioma, (3) pleural effusion, (4) bronchiectasis, (5) fibrosis, (6) cavitation, and (7) dissemination. With the exception of fibrosis and dissemination, all of the complications of coccidioidomycosis create diagnostic problems for the thoracic surgeon.

TABLE I
RESECTION IN PULMONARY COCCIDIOIDOMYCOSIS

Type of Operation	Melick's Modified Series	Authors' Series
Pneumonectomy	4	14
Lobectomy	56	41
Segmental lobectomy	20	35
Pulmonary resection with decortication	7	9
Decortication	1	1
Totals	88	100

The first significant statistical data on surgery in pulmonary coccidioidomycosis were compiled by Melick,[4] who polled all members of the American Association for Thoracic Surgery as well as a large group of other physicians who might have had occasion to perform excisional surgery in treating this disease. Dr. Melick's collected series, modified by withholding from it the data we contributed in our previous paper, is now compared to our current series in tabular form. (Table I.)

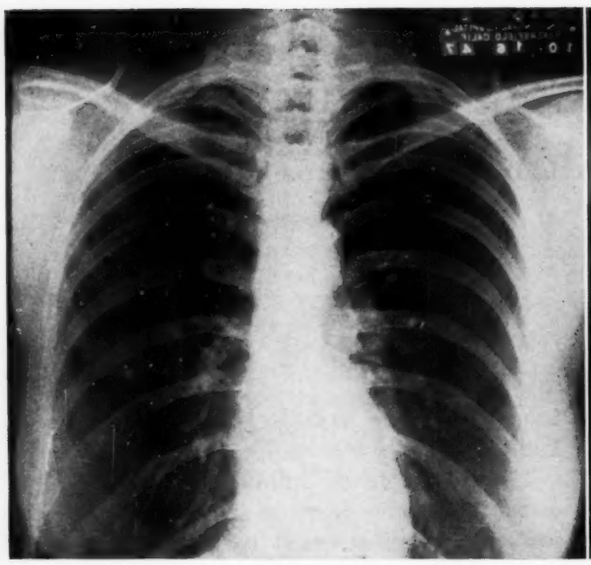

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FIG. 1. Typical thin-walled coccidioidal cavity in the left upper lobe.

FIG. 2. Chronic coccidioidal cavity in left upper lobe that has become a giant cavity. The patient refused operative treatment and died one year later of hemorrhage.

In the 750 cases of pulmonary coccidioidomycosis that were reviewed, 100 patients underwent surgical treatment. From medical observation of these 100 cases, endoscopic examinations, surgical findings and reviews of pathologic specimens, we have evolved the following indications for operation: (1) giant cavity; (2) secondarily infected cavity; (3) check-valve cavity; (4) ruptured cavity (pleural effusion, spontaneous pneumothorax, empyema, bronchopleural fistula, non-expansile lung); (5) coccidioma; (6) hemoptysis (continued, severe). (Figs. 1 to 6.)

COCCIDIOIDAL CAVITIES

Most cavitations are "cyst-like" and silent on auscultation.[5] The acute phase of the cavity appears with the disease's parenchymal infiltration and disappears with resolution of the infiltration. The cavity is then chronic in nature and persists without a zone of fibrosis.

Persistent pulmonary cavities cause the greatest possible concern to the attending physician from the standpoint of diagnosis, prognosis and treatment. Collapse therapy frequently fails. Our postsurgical examinations of specimens showed such failures to result from two conditions. In the first of these the cavity, although appearing thin-walled roentgenographically, was actually enclosed by a dense fibrinous wall that collapsed with difficulty even when subjected to direct manual pressure. In the second condition dense adhesions joined the cavity wall to the thoracic cage. We therefore believe that the treatment of choice is the surgical removal of all existing cavities; otherwise many distressing complications and symptoms may be expected to occur.

If the cavity is under constant medical management, the onset of such complications and symptoms may be postponed for years. However, the word *postponed* is used advisedly. Even under the best medical management it is not at all likely that the complications will be prevented.

The coccidioidal cavity parallels the problem of lung abscess or bronchiectasis. Patients with one of these latter conditions must be kept under constant medical care, with vigorous treatment during upper respiratory infections, and usually they must receive a daily small dose of antibiotic. Similarly, the persistent coccidioidal cavity must be kept under constant symptomatic and radiographic observation. It will eventually be seen to enlarge. Complications will then shortly ensue and resection will be necessary.

The fear that an operation will stimulate dissemination is one of the principal reasons for delaying resection. In this connection it is worth pointing out that dissemination occurs in a ratio of 1:400 cases of all types in the

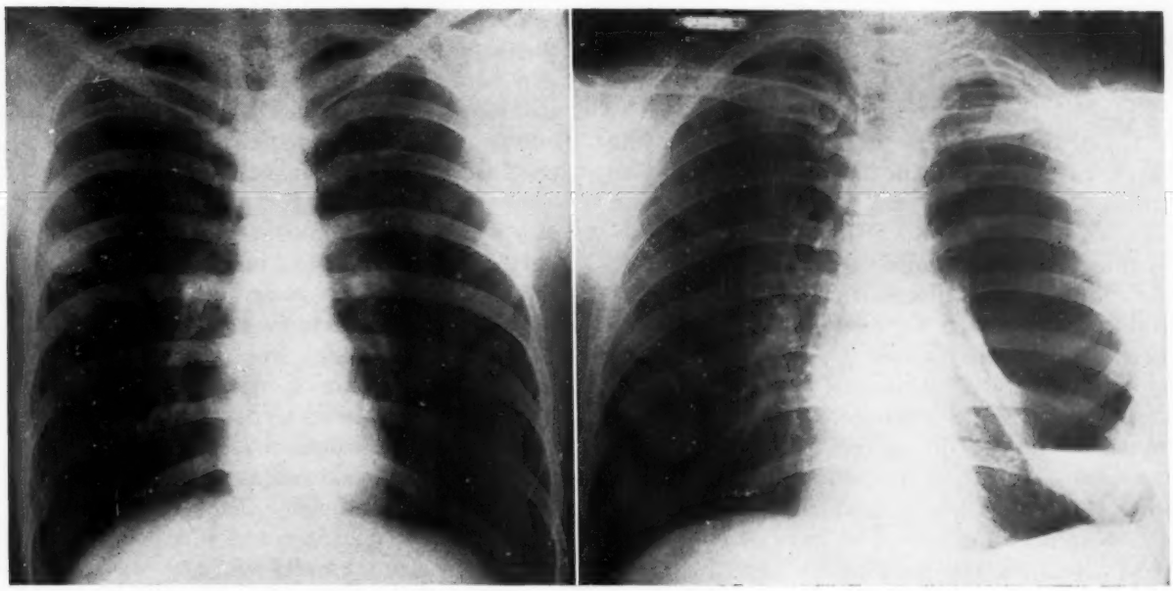

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FIG. 3. A coin lesion in the right upper lobe which proved to be a coccidioma.

FIG. 4. Left spontaneous pneumothorax with persistent bronchopleural fistula and mixed empyema.

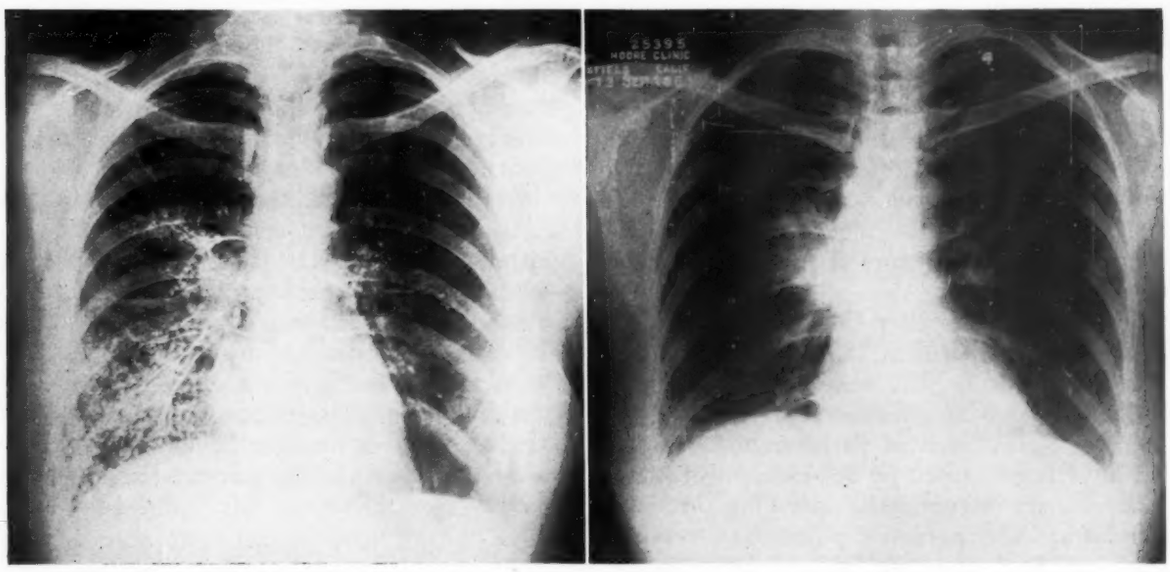

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FIG. 5. Preoperative bronchogram showing a large coccidioidal cavity in the right lower lobe.

FIG. 6. Case of pulmonary coccidioidomycosis which could be confused with bronchogenic carcinoma of the right hilum.

white male (of 1:100 cases in the Negro male), and least often of all in the female unless she contracts the fungus in the last trimester of pregnancy.[5]

The problem of delay as opposed to operation brings us back, then, to the complications which indicated operation.

1. *Giant Cavity.* We have arbitrarily designated any cavity larger than 5 cm. as a giant cavity. A cavity of this size is obviously in need of surgical treatment because of the increased possibility of hemoptysis or of rupture with empyema, or of other severe complications.

2. *Infected Cavity.* We believe that the cause of a cavity's progressive enlargement is secondary infection. The size and rapidity of

cavity formation is directly proportional to the degree, extent and duration of infection. Secondary infections are a common finding and frequently they mask the primary infection.

3. *Cavity with Check-valve Mechanism.* The check-valve mechanism has been explained as arising in either of two ways: (1) as made possible by the membrane formed by secondarily infected cavities; and (2) as being caused by the endobronchial disease that is present in the draining bronchus. In our opinion it is this mechanism which causes a cavity to rupture and bring about subsequent complications. Thus when serial roentgenograms reveal a cavity to be in the process of enlarging, an emergency operative procedure is indicated in order to prevent cavity rupture.

4. *Ruptured Cavity.* The various complications which the ruptured cavity can cause are:

Pleural effusion: This is the most common complication. It occurs as the result of rupture of a small subcortical abscessed cavity. The effusion is treated by aspiration; however, if a thickened pleura develops, surgical intervention is necessary.

Spontaneous pneumothorax: This complication occurs after the rupture of a cavity having a residual large, open bronchus. One can expect associated empyema. Immediate operative treatment is recommended to close the fistula and to clean the pleural space. Decortication as well as closure of the fistula will be necessary.

Empyema: The sooner the empyema undergoes surgical treatment, the fewer technical difficulties will be encountered. In cases of empyema which have persisted for a number of months, a great deal of parenchymal damage will have been caused by secondary infection. This not only increases the operating time but also lowers the patient's pulmonary reserve since increased amounts of pulmonary tissue will have to be sacrificed.

Bronchopleural fistula: In the treatment of bronchopleural fistula—necessarily an operation in an infected field—we have used an extrapleural type of decortication and a wedge removal of the cavity. All patients so treated have recovered without complications.

Non-expansile lung: Two causes are responsible for this condition, namely, pleural effusion which has not been adequately treated and delay in the surgical treatment of a ruptured cavity.

5. *Coccidioma.* A coccidioma is a form of focalized lesion of the pulmonary infection and can be either a true coccidioma or a pseudococcidioma. The pseudococcidioma is a small cavity filled with inspissated material. The coccidioma is a granulomatous lesion of extreme importance, for it falls into the group of so-called coin lesions. It is important not only to the radiologist in differentiating from carcinoma on roentgenograms but also to the surgeon in differentiating from carcinoma at the operating table. In addition, unless the pathologist is aware of coccidioma as a diagnosis, he is apt to designate the specimen a granulomatous lesion or a tuberculoma. Any granulomatous lesion of undetermined etiology should be treated as a suspected coccidioma and the material subjected to culture, animal inoculation and careful scrutiny in order to reveal the spherules of C. immitis.

The three indications for surgical treatment of coccidioma are: (1) when the lesion falls into the group of coin lesions and must be removed for differential diagnosis; (2) when the lesion shows any degree of enlargement, for this is a sign that a secondary infection is brewing; (3) when the coccidioma cavitates, creating the potential of a secondarily infected cavity.

6. *Hemoptysis.* This is our only indication for surgery that is a symptom rather than a pathologic finding. It is a highly important indication, for when hemoptysis occurs there is always the chance of a life-threatening situation as the result of erosion into one of the larger blood vessels. We are familiar with one case in which a large cavity eroded in this manner, causing massive hemoptysis and the subsequent death of the patient.

SURGICAL CONSIDERATIONS

Once the acute phase of the disease has passed, risk of dissemination following surgery is almost negligible.[1] In no instance have we performed surgery for any focalized coccidioidal infection until a full six months or more following the acute stage of the infection. We have seen cavities close during the six-month period, but we have never seen a cavity close after six months. In view of this, we believe there should be a six-month interval between resolution of the acute stage of the disease and surgical treatment.

Our preoperative work-up includes localization of the cavity in an attempt to determine whether or not localized resection will be possible or whether lobectomy will have to be performed. A bronchogram is always done next, for in a great many cases we have found bronchiectasis associated with the cavity or within the area of the infection. We believe that pulmonary coccidioidomycosis is primarily an endobronchial disease, and consequently the chances are good of bronchiectasis being present. Following the bronchogram we wait six weeks before scheduling the patient for the operative procedure.

Operation is carried out in the routine fashion of other pulmonary resections, such operations being performed as lobectomy and segmental or wedge resection depending upon the location of the lesion. Lobectomies are performed by the individual ligation technic as it is used by most thoracic surgeons. Sometimes in performing wedge resection lung tissue around the cavity is found to be infected and the zone of involvement of the lung is greater than the immediate area of the actual cavity. In this case, instead of the wedge resection a segmental resection is performed or a lobectomy. This is done since mattress sutures through infected lung tissue would almost surely result in a bronchopleural fistula. We would rather sacrifice greater amounts of lung tissue than run such a risk.

After a wedge resection the resected lobe is closed in the manner of a fan. Closure is brought about, in both infected and noninfected cases, by a mattress suture which interlocks with the lung tissue, giving the silk suture an appearance similar to the links of a chain. We have found this type of pulmonary tissue closure to be a most effective one even in the treatment of infected pleural cavities.

In all cases of the series diagnosis was confirmed either pre- or postoperatively by one or more of the following laboratory procedures: complement fixation test, sputum examination, culture, animal inoculation or histologic examination.

There has been considerable discussion in the recent literature in regard to complications following operative treatment for coccidioidal infections. Few complications occurred in our series, and we have had excellent results in treating those complications which did occur. This makes us wonder if there are not other circumstances—possibly in the surgical technic, in the evaluation of the case or in some other factor—which may explain the complications that are reported to follow operative treatment.

All of the patients did well in the series except three. There was one postoperative death, and in two patients complications followed treatment. Further cavities developed in these two patients and secondary operations were performed. One patient's second cavity was of tuberculous origin. The other patient's was coccidioidal; apparently either a small cavity was missed at the time of surgery or a small coccidioma "shelled out" to become a large cavity. These two patients, like the others in the series, are now back at work.

COMMENTS

It is occasionally easier to make a diagnosis of coccidioidomycosis *in vivo* than by examination of the pathologic specimen. The coccidioidal cavity allows recovery of spherules from the sputum during the acute phase of the disease, but it may lose its identity in the presence of a superimposed infection of tubercle bacilli or pyogenic organisms. "Masking" of this type may explain the poverty of data in the literature on excisional surgery in the treatment of pulmonary coccidioidomycosis, for it often happens that a case preoperatively considered to be coccidioidomycosis is reported instead by the pathologist as "granuloma, etiology unknown."

The recoveries without complications which followed the operations in this series have been remarkable. Decortication, for instance, was performed in the presence of an active coccidioidal empyema and there was complete reexpansion of the lung, the wound healing by primary intention. These results led us to conclude that suitability for operation is a determination that can be made without regard to the etiology of the pathologic condition and without regard to such problems as whether or not the disease is in a dormant or an active phase.

It has long been known that in cases which involve an extremity alone, amputation can arrest the disease and save the life of the patient. In a somewhat analogous manner, resection for pulmonary coccidioidomycosis can be used to prevent death and is effective in arresting the disease process. Resection

does not cause dissemination to the skeletal and nervous system, and it may even prevent dissemination. Postponement of surgery for fear of dissemination does not seem justified.

Consequently we believe that the conclusion of our preliminary paper is now established: Insofar as the surgeon is concerned in his determination of treatment, all laboratory findings should be disregarded, evaluation being made of the pathologic lesions alone.

SUMMARY

1. The findings are presented of a series of 100 cases of pulmonary coccidioidomycosis treated by surgical methods.

2. Once important only in endemic areas, pulmonary coccidioidomycosis is today a problem of national importance.

3. A review is given of the indications for surgery.

4. The coccidioidal cavity is, like lung abscess or bronchiectasis, an operable condition. Delay of surgery is dangerous.

5. The risk of operation causing dissemination is negligible.

6. Attention is called to the evaluation of the pathologic specimen, particularly "granuloma, etiology undetermined."

7. The rationale for surgery should be based on mechanical considerations, completely disregarding the etiologic agent, C. immitis, or other co-existing pulmonary fungi or tuberculosis.

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The Pathogenesis and Management of Pneumoconiosis

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CERTAIN clinical manifestations are frequently interpreted, as the result of exposure to the inhalation of an air-borne substance, with little or no regard to the presence or absence of any pulmonary abnormality directly due to that exposure. Thus, the manifestations are often labelled as pneumoconiosis without a clear concept of the full meaning of that term and of the requirements essential for its clinical application.

The term "pneumoconiosis" has come to be recognized generally as an entity which is due to the pulmonary deposition of an inhaled particulate substance in the solid phase and has two distinct applications: firstly, as a condition unassociated with any significant pathology or clinical symptoms, and secondly, as a disease accompanied by specific inflammation of the lung and frequently associated with loss of pulmonary function and the occurrence of clinical signs and symptoms of respiratory distress. It will be noted that the definition limits the term to a particulate substance. Therefore living organisms and the majority of organic substances with their respective inflammatory, allergic and toxic effects are excluded.

PATHOGENESIS OF PNEUMOCONIOSIS

The nature of pneumoconiosis is determined by a number of variable factors which operate independently, but which have a reciprocal relationship and which must be appreciated in arriving at a diagnostic opinion. Those factors may be considered according to two major categories, namely, those which pertain to the environment, especially the air-borne particulate substance, and those concerning the person exposed to that environment: *Environmental factors:* (1) physical and chemical characteristics of the particulate substance suspended in the atmosphere at the breathing level of the exposed individual; (2) concentration of the particulate substance in that atmosphere; (3) biologic capacity of that particulate substance, upon inhalation and deposition in the lung, to produce pulmonary damage. *Personal factors:* (1) health status of the exposed individual, especially as it concerns the respiratory tract and particularly the lung; (2) duration of exposure to the inhalation of the particulate substance and its concentration in the lung; (3) inherent variation in the manner in which different exposed individuals respond to the inhalation and pulmonary deposition of the particulate substance.

Physical and Chemical Characteristics of the Particulate Substance. Studies to date indicate that spherical particles greater than 10 microns in diameter are seldom found in the air spaces of the lung. This is apparently due to the fact that particles greater than 10 microns seldom, if ever, remain suspended in the atmosphere for any length of time, or they are too large to pass the filtering mechanisms in the upper respiratory tract and the smaller bronchioles. Thus, the presence of those particles in the atmosphere can be largely eliminated from etiologic consideration. Elongated particles of fibrous material such as asbestos are an exception to that rule. Presumably, the flexibility of these fibers and their ability to conform to the shape and dimension of the small air passage permits them to reach the respiratory bronchioles, and occasionally, the terminal alveolar space.

Air-borne spherical particles less than 3 microns in size are of paramount significance. They constitute, by far, the greatest number discovered in the alveolar spaces and tissue. Particles less than 0.5 micron are particularly dangerous not only because of their ability to remain suspended in the air and to be easily inhaled, but also in view of the experimental evidence that particles of submicroscopic size, at least of certain substances, provoke pulmonary changes which are quite different from

those caused by larger particles having the same chemical composition. For example, when pure amorphous free silicon dioxide is disseminated as a fume with ultimate particles in the order of 0.1 micron or less in size, and inhaled by rabbits, it produces in them diffuse and cellular pneumonitis which is accompanied by early and profound respiratory distress. This series of events does not occur in simple nodular silicosis which results from the inhalation and pulmonary deposition of crystalline free silicon dioxide in particles with a mean size between 1 and 3 microns in diameter.

The chemical composition of the particulate substance to which the individual may have been exposed is, of course, of primary importance in the pathogenesis of pneumoconiosis. The literature is replete with studies of pure particulates and their toxic action on tissues of the body. It is not generally appreciated, however, that the air-borne contaminant may consist of a mixture of substances which necessitate careful analysis before they are quantitatively and qualitatively detected. The mixed contaminant may provoke an entirely different hazard to the lung than either component of the mixture acting as a single agent. The action of one component upon the other may cause agglutination of the particles in the atmosphere. The resulting clumps become too heavy for prolonged suspension and too large for inhalation. A classic example in that regard pertains to a particulate mixture of calcined gypsum which is inert, and crystalline free silica in the form of quartz dust. Furthermore, one component of the mixture may coat the offending particle and thereby minimize or prevent its toxic action upon tissues of the body. This appears to be the mechanism whereby the toxic action of particulate crystalline free silica is inhibited by powdered metallic aluminum or by hydrated alumina. In contrast, the air-borne particulates of a mixture of substances may induce a characteristic and frequently severe inflammatory reaction in the lung. This is the case, for example, in the instance of exposure to the inhalation of zinc beryllium silicate powder with beryllium oxide in the free or uncombined state, and also of particulate carbonaceous material mixed with quartz dust.

Atmospheric Concentration. The concentration of the small particles suspended in the atmosphere at the breathing level of the exposed person is exceedingly important. Obviously, the concentration determines in large measure the number that may be inhaled. Just how high that concentration must be, in the case of a specific aerosol, before demonstrable changes result in the lung are the subject of continued clinical and experimental study. The toxic effects of many particulates have been prescribed in terms of maximum allowable concentration which must not be exceeded if damage to the respiratory tract and lung is to be avoided. The values may not be applicable to every situation and they do not guarantee that health will be maintained on the part of the exposed individual. Furthermore, some of the values are only tentative, pending more definite experience with the respective substance. However, the values do provide a ready bench mark for engineering control measures and for guidance of the industrial hygienist and the physician.

Biologic Capacity. The inherent toxicity of the substance is perhaps the most important of all the factors outlined as determinants in the pathogenicity of pneumoconiosis. Therefore, it is unfortunate that the precise toxicity of an inhaled particulate aerosol is so difficult to ascertain in the human subject. This is true not only because the aerosol may be a mixture of substances, but also because the amount deposited in the lung and the duration of exposure cannot be determined with the desired degree of exactness. In addition, it is impossible to assess toxicity by examination of a single individual who in final analysis may be unusually susceptible or who may not reflect the identical situation involving other individuals exposed to the same aerosol. Therefore, many toxicity studies are based upon inhalation experiments with animals, wherein the atmospheric concentration of the particulate aerosol and the duration of exposure can be controlled and correlated with grades of tissue reaction at definite intervals of time. While many experiments have failed to reproduce abnormal changes identical to those observed in man, it is true that animals provide at least indirect evidence of the probable fundamental principles which govern the toxicity of an atmospheric contaminant for human beings. In the absence of adequate experience with man the experimental evidence is extremely valuable, at least insofar that it affords a guide for the understanding of similar evidence in

man and also serves as a warning against human exposure beyond certain limits.

Personal Factors. Space does not permit an elaborate discussion of each and every factor which pertains to the exposed individual *per se* and which has reference to the pathogenicity and indeed to the management of pneumoconiosis. The importance of the health status of the respiratory tract and lung is obvious. Any abnormality in that status, either functional or pathologic, imposes an additional insult which may severely modify the generally accepted pattern of uncomplicated pneumoconiosis. In this regard one need but recall the effects of increasing age, the adverse influence of chronic bronchitis and bronchiolitis, bronchiectasis, emphysema, pulmonary residuals of past infections, malignancies, and active infections such as tuberculosis. Certainly, such abnormalities must be considered in evaluating the pathogenesis of pneumoconiosis and they should be viewed with extreme caution before attempting a cause and effect relationship.

The duration of exposure bears, in general, a reciprocal relationship to the atmospheric concentration of the particulate aerosol. Within certain limits a short exposure to excessive amounts of an aerosol in effective ranges of particle size will produce the same degree of pulmonary reaction as a longer exposure to more moderate concentrations. An accurate occupational history is essential for an estimation of this time factor. It may be difficult to obtain, particularly when information relative to a man's occupation in any given industry is so varied that a constant exposure to one type of aerosol seldom occurs. A rock driller, for example, gives a history of employment in many different mines or quarries, each of which may involve work in rock of different composition. Even in one mine the occupation of the miner covers many different jobs with exposure to dust from relatively pure ore to those with a high silica content. Some men work exclusively underground, others in surface mills and still others are transferred from one job to another. The aim of the history is to determine as exactly as possible the number of years, months, weeks and days that a workman has spent at various jobs, and to correlate this information with the nature of atmospheric contaminant encountered in each of them. The satisfactory history accounts for every day of his employment and particularly of his exposure to an aerosol.

With respect to the factor of individual variation, it is obvious that not all individuals exposed to a particulate aerosol under presumably the same environmental conditions react alike. Some are susceptible and respond early; others are partly or almost completely resistant. This condition occurs both with the experimental animal and with man. Various explanations have been offered to account for these differences, but none is entirely satisfactory. Inefficient nasal filtration, physiologic peculiarities of the lungs, chronic infection of the respiratory tract, effectiveness of the lymphatic drainage system, quantity of dust deposited in the lungs, particle size, metabolic and genetic factors, and physiochemical differences have been suggested as possible determinants influencing the degree of pulmonary reaction of the individual man exposed to a dusty environment. The physiologic response to climatic factors such as humidity, temperature and barometric pressure have also been considered. The relative importance of each of these elements in the pathogenesis of pneumoconiosis in some individuals and not in others remains to be determined.

With due recognition of these factors it is apparent that, within limits, the types of uncomplicated pneumoconiosis fall into one of two categories, namely, inert or harmless pneumoconiosis and active or harmful pneumoconiosis.

Typical examples of the inert type are those pneumoconioses produced by particles of carbon, iron oxide, cement, gypsum and a host of other agents in pure or mixed state which initiate a reaction no more severe than that caused by any substance foreign to the pulmonary tissue. The pulmonary deposition and the mild tissue reaction in those instances may be regarded often as the fortuitous happenings of everyday life and do not necessarily arise in consequence of a specific occupational exposure.

The manner of primary distribution of an inhaled particulate aerosol in different parts of the normal lung is not entirely clear. Whether that distribution is predominantly subpleural or is confined mainly to the deeper portions of the lung, involving some segments more than others, apparently depends upon a number of physiologic variables including vital capacity, tidal and residual air, and movement of the

lung, diaphragm and chest cage. In any event the inhaled particles that reach the terminal alveoli are taken up by large phagocytes, commonly called dust cells. The function of these actively motile cells is to prevent accumulation of foreign particles in the alveolar spaces. Many migrate into the bronchi and are expectorated. Others find their way into the lymphatic system of the lung and are carried by it to the intrapulmonary lymphoid aggregates and the tracheobronchial lymph nodes. Other phagocytes laden with particles find their way into the interstitial tissue comprising the alveolar walls. There is debate concerning this phagocytic mode of deposition and transport. It appears that some particles gain access to the alveolar tissue without the mediation of phagocytic activity. That theory, if correct, would explain in part diffuse interstitial pneumonitis provoked experimentally by certain substances, such as some amorphous free silica aerosols with an ultimate particle size in the submicroscopic range.

Particulate aerosols that reach the lymphatics are carried along the perivascular and peribronchial trunks to the intrapulmonic lymphoid masses that lie at the dividing points of the bronchi and vessels. Many particles pass through these filter masses and eventually reach the nodes at the hilum of the lung. In cases of prolonged inhalation of heavy concencentrations of an inert dust, these filtering masses may become more or less clogged so that the particles begin to accumulate in the lymphatic channels. Massive exposure of this sort is usually accompanied by enlargement of the tracheobronchial lymph nodes. As with any particulate substance, a slight proliferation of connective tissue takes place both within these nodes and about the afferent lymphatic trunks in the lung. These changes can often be visualized in roentgenograms of the chest as a widening of the root shadows and an exaggeration of the normal linear markings. Such alterations appear only after many years of exposure to high concentrations of inert particulate aerosols. Identical roentgenologic changes may also be seen in long-standing cardiovascular disease and in certain infections; they are also often incidental to old age. Therefore, by themselves they may not be sufficiently characteristic to substantiate a diagnosis of pneumoconiosis.

In regard to the active pneumoconioses it is clinically impossible to assess the capacity of a particulate aerosol to produce pulmonary damage by the examination of a single case. In surveying large groups of men in the same industry who are apparently exposed to the same amounts of active particulates, not all will be discovered to have developed such damage. As cited previously, whether this is due to variations in individual susceptibility, to varying effectiveness of the upper respiratory defense mechanisms, to associated infections, or to differences in exposure which are not detected by existing methods of history taking, is still a matter of debate.

Illustrative of the active or harmful pneumoconioses are those conditions such as silicosis and asbestosis. Each is well established as a specific entity and therefore deserves special attention. It is not intended to refer here to these two particular types in any great detail, but a few aspects will be emphasized to illustrate certain focal points which may assist in the study of other pneumoconioses of the active type.

It was formerly believed that only the crystalline forms of free silicon dioxide caused damage to the pulmonary tissue. In recent years some of the amorphous forms and some of the silicates have come to be regarded with suspicion. One at least—asbestos, a hydrated magnesium silicate—has proved to be definitely irritating. The pulmonary pathology of asbestosis and its appearance on roentgen films is distinct and can be differentiated from that of other pneumoconioses. It causes a diffuse obliterating fibrosis which starts as collar-like sheaths about the terminal bronchioles. With increasing exposure and as the disease advances the fibrosis extends peripherally into the parenchyma of the lung, often producing associated chronic fibrous pleuritis. The tissue response is never nodular as in silicosis. The fibrosis imparts to the chest roentgenogram a faint diffuse haziness throughout the lower lung fields, which in the advanced cases has an appearance comparable to that of ground glass. Occasionally, there are scattered granular and mottled shadows but they do not present the sharp definition of silicotic nodulation.

Particles of pure crystalline silica, when inhaled into the lung, are first acted upon in the same way as is the case with an inert particulate substance. The particles are phagocytosed by large mononuclear cells that eventually find

their way into the alveolar tissue and the lymphatic system of the lung. At this point, however, the tissue response becomes totally different. Whereas inert particulates initiate little or no reaction within the lung, silica dust stimulates the tissue cells and produces an inflammation followed by proliferation of connective tissue. Since the dust particles are transported into the lymphatics early, the first detectable evidence of this reaction appears in the lymphoid tissue about the vascular tree and in the lymph nodes at the root of the lung. As these changes proceed, the efficiency of the pulmonary lymphatics as a draining and filtering system becomes impaired and inhaled silica particles can no longer be eliminated effectively from the alveolar spaces. The dust-laden phagocytes tend to accumulate in all parts of the lung, first in and about small peripheral masses of lymphoid tissue and later in the alveolar septa themselves. The silica particles thus become concentrated at focal points, a chronic inflammation occurs, connective tissue forms and a characteristic silicotic nodule of hyaline fibrotic tissue results. With continued inhalation of silica the number and size of these nodules increases. In the course of time, barring infection, the lung becomes studded with uniformly scattered, firm circumscribed nodules of fibrous tissue.

The pathologic condition in the lung can now be recognized as silicosis on the roentgenogram, which is the most reliable basis for a clinical diagnosis. This is the stage of "nodulation" with discrete shadows, rather uniform in size, density and distribution, scattered throughout all portions of the lung fields. In late stages the development of emphysema at the bases often disturbs the uniformity of the distribution.

Not all silicotic conditions of the lung are manifested by simple nodule formation. In many instances massive areas of fibrosis are present in one or more parts of the lung. They are frequently bilateral and may be symmetric or asymmetric in distribution.

The reason for the development of such areas is often difficult to determine and is still a subject of debate. Some observers are of the opinion that these massive lesions result from conglomeration of previously existing discrete nodules of simple silicosis. It cannot be denied that with continued inhalation of silica some nodules do increase in size and fuse locally to form small conglomerate foci. Lesions of this type, however, are scattered throughout the lung and seldom become large enough to be confused with the massive areas of fibrosis. If lesions of the latter type are the result of fusion of discrete nodules, they should have numerous points of origin scattered throughout the lung and eventually result in uniform and complete fibrosis of the entire organ. It may be argued that a small portion of the lung received more dust than another and consequently a massive lesion developed. To justify this view it must be demonstrated that more inhaled silica particles are deposited in certain areas of the normal lung than in others. Observations on the lungs of experimental animals and those of early cases of uncomplicated human silicosis which come to autopsy have failed to substantiate this view. They have likewise failed to confirm the opinion that localized atelectasis of the pulmonary tissue is the factor responsible for the diffuse fibrosis.

A third possibility is the effect of other minerals associated with silica. It is known that such dusts tend to accumulate at the periphery of silicotic nodules where they produce the formation of more or less cellular connective tissue. Fusion of such reactions about contiguous nodules might conceivably be responsible for conglomerate foci. But if this is true, such a process should result in diffuse generalized fibrosis.

The most likely explanation for massive lesions of fibrosis is that they occur in regions of the lung which have been injured by infection. Such injury leaves residual granulation or scar tissue and impairs the lymphatic drainage so that inhaled silica particles can no longer be eliminated effectively from those regions. Accumulation of carbonaceous pigment or other particulates in pulmonary scars is well illustrated in specimens with apical foci of healed tuberculosis. A common finding about almost any fibrotic or calcified tubercle is a peripheral zone of dust pigment often so concentrated as to obscure the microscopic characteristics of the lesion. A similar change is also observed about many other scars of unknown etiology. These observations lead one to believe that particles of inhaled dust accumulate in certain areas of the lung, not because more arrive at the focus but because fewer are eliminated by way of the lymphatic system. The result is a localized accumulation of dust. When the dust

is silicious, the excessive local concentration exerts its maximum effect; an unusual number of nodules develop and diffuse fibrosis results from the action of the silica on any pre-existing scar tissue.

The majority of the massive fibrotic lesions of advanced silicosis are associated with foci of infection within the lung. In most instances the etiologic agent is the tubercle bacillus. When such lesions first develop the infection is most often latent; scar tissue continues to form at its periphery and the area increases in extent. Ultimately the silica reactivites the encapsulated focus harboring the bacilli and the infection spreads very slowly. Foci of this kind, which are due to the combined action of tubercle bacilli and silica, are generally designated as tuberculosilicosis.

In many cases it is difficult to obtain clinical evidence of a bacillary infection within such lesions. The usual picture of uncomplicated phthisis is frequently absent and the sputum often remains negative for acid-fast bacilli even after examination of numerous specimens. Repeated guinea pig inoculations are often necessary to demonstrate a positive sputum.

Generally, however, if the larger number of these massive lesions are followed long enough, they will eventually reveal definite evidence of tuberculosis. Although delayed, the clinical symptoms and signs of infection will make their appearance and serial chest roentgenograms will show extension of the shadows which may ultimately go on to cavity formation.

The presence of active infection within these lesions has been verified by autopsy. Anatomically such lesions appear as irregular masses of firm grey or black fibrous tissue with linear extensions into the surrounding lung. Often they extend to the pleura and are accompanied by dense pleuritic adhesions. The tuberculous complication within the mass is identified by scattered islands and bands of granulation tissue, foci of caseation in various stages of organization, or by cavity formation. The clustered tubercles of bronchogenic spread or the widely scattered lesions of hematogenous dissemination are much more uncommon in tuberculosilicosis than in simple phthisis. Apparently the massive fibrous tissue traps the tubercle bacilli and prevents their spread to distant foci.

Not all manifestations of tuberculosis in the silicotic subject are of the massive fibrous type. There are cases in which the infection localizes in and about pre-existing silicotic nodules. The center of the nodule becomes caseous and a zone of tuberculous inflammation is seen about its periphery. This change results in an increase in size of the nodule and a loss of its sharp definition. Roentgenologically the discrete nodular shadows seen in uninfected silicosis now have fuzzy indistinct borders. This form is referred to as the "perinodular type." Clinically it is manifested by early symptoms of intoxication, the presence of bacilli in the sputum and early termination.

Although tuberculosis is the most frequent complication of silicosis, other forms of pulmonary disease may also be involved. Non-specific chronic bronchitis and bronchopneumonia are perhaps more common than in the non-silicotic individuals. In certain industrial groups, notably foundry employees, the increased incidence of pneumonia has been attributed to the extreme changes in temperature and humidity rather than to the inhaled dust. Experimental evidence fails to show that inhaled particulate silica has any influence upon a pneumococcal infection. Bronchial spirochetosis occasionally complicates silicosis. However, that infection responds favorably to treatment and appears to be incidental to the deposition of particulate silica in the lung. Pulmonary carcinoma has been attributed to the irritating properties of inhaled silica, but there is no real evidence that such malignancy is more frequent in silicotics than among subjects of the general population. To date, therefore, it has not been satisfactorily demonstrated that these particular complications bear an etiologic relationship to inhaled particulate silica.

In addition to silicosis and asbestosis other special forms of active pneumoconioses could be cited. These would include pneumoconiosis in coal miners, diatomaceous earth workers, certain foundry employees, operators of induction furnaces, and in subjects exposed to particulate aerosols of cobalt, cadmium, manganese dioxide, chromates, bauxite and beryllium oxide. The pulmonary changes attending some of these various pneumoconioses are fairly well identified. Their relation to the etiology and pathogenesis of pulmonary disease has received considerable attention. For many of them, however, the body of evidence in regard to their action is not as great as with silicosis and asbestosis.

MANAGEMENT OF PNEUMOCONIOSIS

Prevention remains the only reliable means for combating pneumoconiosis. Thus far, specific therapeutic measures have not been discovered which have an appreciable effect upon an established pulmonary process resulting from the deposition of particulate aerosols in the lung.

The field of prevention involves the collaborative effort of many persons, not only the exposed subject but also individuals with special abilities who represent a number of professions. These include physics, chemistry, engineering, the social sciences, hygiene and medicine. The major burden of responsibility in this regard rests upon the industrial hygienists and the physician.

The industrial hygienist is in a most favorable position to identify and to define a potential or actual health hazard possibly due to a particulate aerosol. He, better than anyone else, is well acquainted with various instruments and technics for the collection and study of those aerosols. Furthermore, the industrial hygienist can ascertain the particular operation responsible for generation of the aerosol and thus can introduce precise measures for its control or elimination. He knows the work habits of the men and can determine the frequency and duration of their exposure.

The physician's part in prevention is equally important. His study of the lungs of individuals gives evidence of a respiratory hazard possibly due to the inhalation of a particulate aerosol. Accordingly, he can detect those individuals already afflicted and can introduce therapeutic measures for their improvement. He can appraise the nature and extent of their pulmonary impairment, and thus give guidance for compatible activity and work. But more important, the physician can assist in the selection of individuals free from pulmonary disease who otherwise may be incapable of withstanding exposure to an atmospheric pollutant.

The diagnosis and management of pneumoconiosis are contingent upon the following: (1) evidence of disease in the lungs demonstrated in the roentgenograms; (2) physical examination and other medical study to determine the nature and extent of pulmonary involvement and associated disability; and (3) a history of exposure to a particulate aerosol adequate to produce pulmonary disease and to impair health.

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AFTER total gastrectomy re-establishment of continuity may be attained by isolating the second loop of jejunum (supplied by the second intestinal artery) and anastomosing its proximal end to the esophagus and its distal end to the duodenum, end-to-end. At the esophagus, the anastomosis is usually end of esophagus to side of the jejunum, after closing the proximal jejunal opening. Jejunal repair, after isolation of the above loop, is by end-to-end anastomosis. If the mesentery is too short to permit the aforementioned procedure, continuity can be established by Roux's Y-operation. Even in this latter procedure surgeons close the proximal jejunal opening and anastomose the end of the esophagus into the side of the jejunum. Of course, the duodenal stump has previously been closed. (*Richard A. Leonardo, M.D.*)

Silicosis and Asbestosis

DIAGNOSIS, PREVENTION AND TREATMENT

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ALTHOUGH dust disease of the lungs can be traced far back in history, it did not become a serious problem until the introduction of mechanical processes in mining and manufacturing which greatly increased the amount of dust generated. Engineering methods of protecting those exposed did not keep pace with the increasing speed of production. Little thought was given to the early disabilities and deaths which were variously termed "consumption," "phthisis" and so on, and which in reality were cases of silicotuberculosis or advanced asbestosis. The diseases were thought to be inherent in the industries and a part of the risk assumed by a worker when he entered such fields. Not until the whole problem suddenly burst upon the public consciousness, through civil suits and newspaper publicity, did many industrialists realize that something had to be done.

Similarly, medical science was unprepared for this epidemic of occupational diseases and its resulting hysteria. We know how meager the teaching of occupational diseases of all kinds had been in our medical schools until recent years, except for lead poisoning which came to light much earlier in the industrial era, probably due to the much shorter period of exposure required for the disease to develop and the dramatic onset of its symptoms. Silicosis and asbestosis, on the other hand, are slow in their development, requiring years of exposure to atmospheres sufficiently high in silica and asbestos dust to produce even a recognizable change on the chest roentgenogram. Furthermore, the onset of symptoms is far from dramatic, except for the few cases of silicotuberculosis which come to light with the first hemoptysis. However, the greatest factor in delaying our recognition of the condition was the lack of good diagnostic chest roentgenography until about twenty-five years ago. The chest films used in 1915 in the first silicosis survey in the United States, made in the Missouri lead mines, showed only the grosser lung lesions and none of the finer details which we consider so essential for accurate diagnosis today.

Silicosis remains the principal occupational disease of the lungs from the standpoint of numbers of workers involved because of the many industries which have had exposure to dust containing free silica, SiO_2. The major ones have been foundries, granite operations, sandblasting, mines containing quartz rock and sandstone wheel grinding. Some of these no longer are causing silicosis because of the remarkably improved dust control in the past twenty years and the replacement of sandstone with the artificial abrasives. The diagnosis of silicosis must be based on three fundamental criteria: first, the characteristic nodular x-ray pattern; second, medical history and history of adequate exposure to dust containing crystalline-free silica; third, physical examination, laboratory and physiologic studies to determine if the silicosis has caused functional disturbance of the lungs.

The nodular x-ray pattern due to individual fibrous nodules differs somewhat with the various silica exposure industries, depending upon the type and degree of the other components of the dust which tend to modify the silica reaction. The root shadows, however, usually are enlarged and increased in density because of enlarged and fibrotic root lymph nodes. This finding differentiates silicosis from siderosis or iron pigmentation which also causes a nodular x-ray pattern, but with which the root lymph nodes are not enlarged or increased in density. Also, the generalized nodulation with siderosis usually is more discrete and never becomes confluent as silicotic nodulation occasionally does. When silicotic nodules become conglomerate, other nodular shadows in the lungs may become less and less apparent as compensatory emphysema develops.

Just as silicosis cannot be diagnosed during

life unless the roentgenogram shows evidence of nodulation, of equal importance is the history of sufficient exposure to dust which is capable of producing silicosis. This is essential because there are some twenty different conditions and diseases which may look exactly like silicosis on a chest roentgenogram. Some of these are siderosis and hemosiderosis, some fungous infections, non-specific pneumonitis, miliary tuberculosis, berylliosis, some forms of asbestosis, miliary metastatic carcinoma, mitral stenosis, sarcoidosis and polycythemia vera. Because of the great similarity of the x-ray pattern of these conditions and silicosis, it is obvious that the latter cannot be diagnosed by x-ray alone.

A detailed occupational history is an absolute essential with all nodular x-ray patterns. This should start with the worker's first gainful employment. Any jobs which involved dust exposure require detailed questioning regarding the type and degree of the dust. It is not enough to say that a man has been a foundry worker or miner. One must query: What kind of foundry or mine? What job or jobs did he do? If a grinder, what was being ground and what was the composition of the abrasive wheels? If the wheels were made of an artificial abrasive rather than sandstone, silicosis cannot develop unless the castings being ground had sand scale on their surfaces. With mining, silicosis cannot develop unless there had been drilling and blasting in rock containing more than 10 per cent crystalline-free silica. These and many other details must be inquired into before any conclusions should be drawn. No matter how suspicious the x-ray appearance, unless there was exposure to quartz or other crystalline-free silica dust in particle size ranges of 5 microns or less, in concentrations of more than five million particles for cubic foot and for time intervals of more than ten years, a diagnosis of silicosis is unwarranted. The dust concentrations needed to produce silicosis vary inversely with the free silica content. Most states now have codes defining the relative dust concentrations which may be considered safe.

The medical history also is important for the diagnosis of silicosis. The first and sometimes only symptom of disabling silicosis is a slowly increasing shortness of breath on exertion. A dry or productive cough may or may not be present. When this is marked and accompanied by a recognizable wheeze in the chest, bronchial irritation and obstruction usually are the cause, which may or may not be related to the silicosis or dust exposure. Early discrete nodular silicosis usually causes no symptoms referable to the chest. When such symptoms are marked in the presence of minimal nodular silicosis, other causes should be looked for. Silicosis also does not cause loss of weight unless accompanied by active and open tuberculosis. There may or may not be any chest pain with advanced cases and there is usually none with early cases. When chest pain is present, it ordinarily is due to excessive coughing rather than to the silicosis *per se*. Weakness, hemoptysis, digestive disturbances, night sweats, insomnia, dizziness and edema of the extremities are not characteristic of uncomplicated silicosis.

A complete physical examination and laboratory and lung function studies are also needed before an opinion on the presence or absence of disabling silicosis can be given. Objective signs on physical examination are few. Changes in the appearance usually are not indicative of silicosis *per se*. Decreased chest expansion usually is found only in advanced and complicated cases. Physical examination of the chest is made primarily to determine if there is airway obstruction, emphysema, or active infection. Simple nodular silicosis usually reveals no chest abnormalities. Evidence of cyanosis and clubbing of the fingers also should be looked for and may be present with advanced and long-standing cases.

There are no laboratory studies which are diagnostic of silicosis. The finding of silica crystals in the sputum suggests that the individual has had some silica dust exposure, but not that he has silicosis. The same is true of the finding of silica in the urine. The blood count shows nothing characteristic in silicosis except for one or two unverified reports of an increased eosinophilia count. Sputum and gastric cultures for tubercle bacilli and fungi are necessary if the roentgenogram suggests the possibility of complications. The blood sedimentation test is useful with periodic examinations to determine if active tuberculosis is developing as a complication. Simple nodular silicosis does not cause an increased sedimentation rate.

Lung function studies have become increasingly valuable in recent years in determining the extent of ventilatory impairment

in silicosis, if any. In general it may be stated that simple nodular silicosis usually reveals no measurable impairment of lung function unless accompanied by obstructive and unrelated emphysema. Emphysema of a significant degree usually does not result from silicosis unless the latter is advanced. Other causes for emphysema should be sought when it is found in a worker who has no more than minimal to moderately advanced simple nodular silicosis.

The most reliable lung function tests of the simpler variety are the timed vital capacity and maximal breathing capacity determinations. Both have been found to correlate well with residual air determinations, which usually do not need to be made. Both of these tests, however, require a maximal effort on the part of the person being tested, which is difficult to obtain in many controverted patients. However, when the tester breathes with the patient and continues to encourage him to give a maximal effort, reliable figures are obtainable. Blood arterial oxygen saturation determinations are advisable both before and after exercise when the maximal expiration is consistently longer than 3 seconds and the maximal breathing capacity is materially below 100 L. per minute. Besides these lung function tests it often is valuable to determine the maximal excursion of the diaphragm, preferably recorded on a double exposure film. Advanced silicosis and obstructive emphysema usually result in a significant decrease of the maximal diaphragmatic excursion, but simple nodular silicosis does not.

Prevention is the most important feature of this preventable disease and two aspects are recognized. First, silicosis can be prevented by proper dust control, which includes exhaust ventilation, substitution of wet methods for dry, replacement of silica materials with non-silica and the use of protective equipment. These preventive measures are effective as proved by the complete absence of new roentgenographic evidence of silicosis in an increasing number of silica-exposure industries in the past twenty years.

The second aspect of prophylaxis is the prevention of disability in those who already have some silicosis. This necessitates accurate differential diagnosis because of the benign pneumoconioses (particularly siderosis), which may simulate silicosis by x-ray but which never became disabling. The first advice which many physicians give their patients who are found to have nodular roentgen changes is that they leave their jobs. Experience shows, however, that even those with early silicosis should be kept at the work they were trained to do and every effort made to reduce the silica dust dissemination on their jobs to a minimum. The only exceptions should be those patients with progressive tuberculosis or silicotuberculosis who either must be isolated if infectious or placed at light non-dusty work if not.

Fear caused by well meant but usually overexaggerated advice regarding the extent of the silicosis has caused more disablement in some trades than have the lung changes themselves. Such iatrogenic or doctor-induced disability is as real to the patient as are the symptoms from advanced lung disease. Workers with minimal silicosis need assurance that there is little danger of their lung changes progressing to a dangerous stage with the improved dust control. With few other diseases is the psychologic approach more important.

Only those cases which are advanced or complicated by tuberculosis or emphysema require treatment. In the author's experience less than 10 per cent ever become sufficiently disabling to require therapy and such cases are becoming fewer each year as preventive methods of the past two decades are showing their effectiveness.

Advanced cases of silicosis, which usually have considerable emphysema if disability is a factor, can be materially improved symptomatically by methods which promote drainage of retained bronchial secretions. Bronchodilator drugs, such as neo-synephrine® (1.5 cc. of 0.5 per cent) or isuprel® (6 to 8 drops of 1:200 solution), when placed in a nebulizer with 100 per cent oxygen and inhaled with the intermittent positive pressure technic proposed by Motley, have given very effective results. The resulting improved ventilation, although temporary, has caused such a frank improvement in the morale and feeling of well-being of many coal miners that this form of therapy is recommended for disabling silicosis and emphysema from any cause. Courses of treatment may have to be repeated at rather frequent intervals, depending on the severity of the case.

Other measures which must be a part of the therapeutic regimen are prevention and active treatment of colds and other respiratory infec-

tions, prevention as far as is possible of contacts with active cases of tuberculosis, and discouragement of smoking to reduce bronchial irritation and secretion to a minimum. Any measures which will prevent bronchial obstruction are indicated. The cough reflex, therefore, should not be subdued and codeine should be withheld unless the cough is severe. Maintenance of the general nutrition of the patient also must be part of the treatment program. Continuing graded exercise is especially necessary to prevent further atelectatic areas of the lungs from developing. Support of the lower abdomen with its resulting support of the diaphragm will improve ventilation in many patients with advanced non-obstructive emphysema, but is contraindicated when there is considerable bronchial obstruction. Aluminum dust inhalation has been disappointing as a form of therapy except for some psychologic improvement in occasional cases.

The relationship of silicosis and tuberculosis has been recognized for many years. Most clinical and laboratory studies have shown a higher incidence of pulmonary tuberculosis in persons with silicosis than in the general population. Tuberculosis, however, is the only lung infection which appears to be more prevalent with silicosis. Such combined lesions of silicotuberculosis usually are more chronic than is tuberculosis alone and they tend to progress with an increasing overgrowth of fibrosis. Tubercle bacilli commonly are not liberated in the bronchial tree for many years and occasionally never. Sanatorium care is not only unnecessary but also inadvisable until the sputum or gastric contents show tubercle bacilli. Streptomycin, P.A.S. and I.N.H.® are no more effective in chronic closed silicotuberculosis than they are in chronic fibroid tuberculosis, but when the infection is open the patient should be treated precisely the same as a patient with active tuberculosis. Surprising remissions have resulted from such therapy even in the presence of considerable silicosis.

The decided reduction in the past twenty years of the dust exposures in the dusty trades is having a profound effect on the development rate of both silicosis and silicotuberculosis, to the extent that today new cases of silicotuberculosis are no longer seen except in the older workers who had exposure to the heavier dust concentrations in the past. The increasing discovery and isolation of persons with active tuberculosis in the community as well as in industry also is helping to prevent new cases of silicotuberculosis, to such an extent that it soon will cease to exist as an occupational disease. The pessimism of the past regarding the prognosis of silicosis should be replaced by a more optimistic outlook in the vast majority of cases, and those affected should share in that optimism.

Asbestosis is a specific fibrosis of the lungs due to the inhalation of asbestos fibers, which chemically are a hydrated magnesium silicate. They do not contain any free crystalline silica. They appear to cause a mechanical plugging of the respiratory bronchioles and the longer fibers are more pathogenic than shorter ones. Fibers less than 10 microns in length have been shown not to cause the disease in laboratory animals. The characteristic asbestos bodies seen under the microscope in asbestosis lung sections are asbestos fibers with deposits of blood cells and blood protein on their surfaces. The lung fibrosis resulting from these fiber inhalations appears to start as collars of fibrosis around the plugged bronchioles. Whorled fibrous nodules which are the unit lesions in silicosis are rare, but occasionally are seen in areas of advanced fibrosis.

As with silicosis the diagnosis of asbestosis must be based not only on the x-ray pattern but also on adequate history of exposure plus physical and laboratory findings. The x-ray pattern with this disease is somewhat unusual and not as clearly defined as with nodular silicosis; an indefinite haze over the lower lobes appears early, which progresses by slow increase in density and a gradual disappearance of the vascular shadows. Some patients seem to progress through a soft and rather discrete nodular pattern. Pleural adhesions which tend to increase are seen frequently, giving the common "shaggy heart" appearance. The typical haze has been referred to as a "ground-glass appearance." Advanced cases commonly show marked emphysema and blebs.

Because of the indefinite character of the x-ray pattern, the film technic must be of top quality with this disease. Too often underexposed films and those with blurred vascular details due to too long exposure time are misread as showing asbestosis. The films of markedly overweight persons also are often misdiagnosed for the same reason. In addition, conditions which may simulate asbestosis by

well taken x-ray films are chronic passive congestion, bronchiectasis, polycythemia and infiltrating malignant metastases from the mediastinum.

Without a history of adequate exposure to asbestos fibers, a diagnosis of asbestosis cannot be justified. Prolonged exposures for more than fifteen years usually are necessary before x-ray evidence of the disease becomes apparent, except where concentrations of the dust are extremely high. If the laboratory evidence of the long fibers being the primary cause of asbestosis is valid, the permissible dust counts which have been established for the prevention of asbestosis are entirely incorrect. All are based on the number of fibers per cubic foot which are less than 10 microns in length, which it now appears are innocuous. More detailed laboratory studies to establish permissible concentrations of harmful amounts of asbestos fibers seem to be indicated. Until these are available only rough estimates of safe limits of dustiness with asbestos fibers must suffice.

The medical history of asbestosis is quite similar to that of disabling silicosis, in that shortness of breath on exertion is the most striking symptom. There is a general belief, however, that minimal changes by x-ray are more disabling with asbestosis than with silicosis. Whether or not this is true remains to be demonstrated. Cough and expectoration are not characteristic symptoms and when present are most likely due to other causes. The same is true for pain in the chest.

As with silicosis, prevention of asbestosis involves not only a reduction of asbestos dust exposure in the working environment but also reassurance of those patients who have minimal x-ray changes that these findings are of no significance, provided their future exposure to asbestos dust is minimal. Unlike silicosis, asbestosis does not seem to progress after the dust exposure stops or is materially reduced. In the author's experience numerous cases of asbestosis diagnosed as first and second stage in 1943 had not progressed visibly by 1953 in spite of these workers continuing their regular jobs in an asbestos textile plant under markedly improved conditions of dust control.

As for treatment, symptomatic relief of disabled patients most likely cannot be effected with the same therapy suggested for disabling silicosis. Bronchospasm and retained bronchial secretions seems to be much less apparent factors in disabling asbestosis than in disabling silicosis. This looks like a paradox since the basic pathologic change appears to be bronchiolar obstruction, but this obstruction looks more irreversible. Effective therapy for disabling asbestosis has not been demonstrated.

As for complications, unlike silicosis, American experience has not shown any increased incidence of tuberculosis with asbestosis. Also, recognized American cases of asbestosis have not shown any more lung cancer than that in the general population, although British experience suggests that there may be a causal relationship.

In conclusion, silicosis and asbestosis are preventable diseases. Experience in the past ten years has shown not only a decreasing incidence of new cases as recognized by x-ray, but also fewer and fewer affected workers are becoming disabled. This is due not only to lower and lower dust exposures in most industries but also to lessened opportunities for tuberculosis contacts in our communities and industries, and to an even greater extent to an increasing optimism on the part of the medical profession on the prognosis of these dust diseases. The pessimism of the past is being replaced by the realization that a diagnosis of silicosis or asbestosis is compatible with good health and a feeling of well-being.

Beryllium Poisoning (Beryllosis)

X-RAY MANIFESTATIONS AND ADVANCES IN TREATMENT

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THE term "beryllium poisoning" is all-inclusive and may be liberally interpreted as any pathologic condition resulting from exposure to beryllium. By way of definition, beryllosis (beryllium poisoning) is a general disease characterized clinically by pulmonary insufficiency and having the major pathologic changes in the lung. It results from the inhalation of finely divided beryllium compounds. The characteristic lesion is a granuloma. The clinical course of beryllosis ranges from acute to chronic, and for the purposes of this discussion we will limit ourselves to the chronic type of the disease which is the more prevalent and the more difficult to manage.

Possibly as many as 500 cases of chronic beryllosis have occurred in the United States since the first reports of the disease in 1946. Of this group over 100 have been exposed to beryllium in fluorescent lamp phosphors alone, the remainder to a variety of products containing beryllium. Epidemiologic studies indicate that there was a potential exposure to beryllium oxide proved in all these cases, which was not true for the other compounds of beryllium. It followed, therefore, that beryllium oxide (actually the presence of free beryllium oxide) was the common denominator in causing chronic beryllosis.

The pathologic anatomy in chronic beryllosis is characterized by diffuse granulomatosis very much like sarcoidosis. The lungs are voluminous and emphysematous with scattered fine nodules, and diffuse fibrosis, which is interstitial and nodular and is associated with the granulomatous reaction. Giant cells are prominent in the picture and are of the Langhans type.

The symptoms at the time of onset of the chronic disease may be variable. Following termination of exposure, the onset is often delayed from months to a period as long as eleven years before the appearance of symptoms. However, it is not uncommon to find roentgenologic changes preceding clinical symptoms by as much as two years. The first clinical symptoms may be mild with vague indisposition, slight but persistent weight loss, weakness, easy fatigability and occasional cough (usually non-productive and occurring most frequently in the mornings). Exertional dyspnea may often be the presenting symptom. Cyanosis and clubbing of the fingers is a frequent observation in advanced chronic cases. Sooner or later symptoms of cardiac decompensation add to the distress of the patient, ending up with chronic cor pulmonale. Rapid and shallow breathing is characteristic, and in chronic beryllosis the alterations are similar to the disturbances seen in silicosis or cardiac disease. Interstitial changes in the lung disturb the Hering-Breuer reflex, and the variable shunts will also have varying effects upon the patient's vital capacity. Significant reduction in vital capacity may be expected from engorgement of the pulmonary vessels alone. With pulmonary hypertension and right heart strain, there is often engorgement of the liver which may lead to abdominal pain, nausea and vomiting, giving the impression of general intoxication. The essentials for diagnosis of beryllosis are: (1) Occupational history of significant exposure to beryllium compounds; (2) a characteristic type of onset and clinical disease; (3) radiologic findings consistent with beryllosis; (4) clinical laboratory findings consistent with the disease; and (5) chemical findings of beryllium in tissues or urine. Because of the similarity of the granuloma of beryllium with that of sarcoidosis, diagnosis by biopsy is not always completely definitive.

Although the radiologic changes have certain definite characteristics, the x-ray alone will not and should not serve as the single factor to determine the diagnosis. All of the patterns, including the fine discrete granularity and nodularity from 2 to 5 mm. and the enlargement of the tracheal bronchial nodes, can be simulated by other diseases. However, clear-cut

roentgenographic signs in the early stage of the chronic disease are characterized by diffuse finely granular haziness with some degree of obscuration of the parenchymal markings. With advance in time the finely granular shadows later take on a fine nodular aspect, simulating miliary tuberculosis, and between these shadows lobular emphysema is evident. Later on there is a tendency toward a confluence of the smaller nodules with larger nodules appearing. These do not reach the size seen characteristically in late silicosis, but they may approach this picture. Occasionally, the nodularity along the bronchial tree is quite marked, and the roentgen pattern is indistinguishable from that of early silicosis. In the more characteristic diffuse nodular roentgen picture the lesion must be distinguished from miliary tuberculosis, from radiopaque deposits such as siderosis and stannosis, and from the finely granular appearance occasionally seen in the rheumatic diseases.

For purposes of convenience many clinicians divided the chronic beryllosis x-ray pattern into three stages: (1) *The stage of granularity*, which is a finely granular diffuse haziness with some sparing of the apices and extreme bases where there is often compensatory emphysema. (2) *The stage of reticulation*, when a reticulant-type pattern is superimposed on the Stage 1 granular background. Often there is slight fuzziness and enlargement of the hilar areas. (3) *The stage of nodulation*, when there is distinct nodulation up to 5 mm. in size which does not coalesce, cavitate or calcify and gives the appearance of a large flake "snow storm." Cor pulmonale with right-sided cardiac enlargement is common at this stage.

TREATMENT

Chronic beryllosis is one of the progressive disabling types of diseases which has been resistant to practically all forms of therapy. Prior to the advent of ACTH and cortisone, the treatment was completely symptomatic and supportive. Pulmonary insufficiency requires frequent or consistent use of oxygen even at rest. In mild cases general supportive treatment with exercise to the limit of comfort is indicated; in the more severe cases bedrest and continued oxygen therapy are necessary. Penicillin-streptomycin-aerosol therapy is of value in dealing with intercurrent infections but does not appear to alter the course of the underlying disease. Specific treatment designed to aid in the elimination of beryllium, such as BAL and solubilizing agents, have been without effect.

With the advent of cortisone distinct improvement both symptomatically and by metabolic tests is evident. Less accessory oxygen is required. There is increased vital capacity, return of energy noted, improved appetite, weight increase, reduction in dyspnea and cough, heightened morale, and some degree of regression of the lesions noted roentgenologically. The regression is reversible when therapy is stopped. However, over the course of the past several years it is quite apparent that corticosteroid therapy will not effect a cure in chronic beryllosis but very definitely will make the patient more comfortable and possibly retard and prevent progression of the disease to a more fibrotic state. The evident symptomatic improvement, the x-ray changes and the sense of well-being induced by corticosteroid therapy have warranted its continued use and, thus far, has provided the one single modality which has been of some benefit to these patients.

Further research in the field of therapy has shed light on the promise of utilizing chelating agents which might either filter out the accumulated beryllium or immobilize the beryllium so that it cannot be further instrumental in producing pulmonary changes. Dr. J. Schubert of the Argonne National Laboratories has been most instrumental in producing a chelating drug, ATA (Aurin Tricarboxylic Acid), which at this stage of its development appears to be toxicologically safe and theoretically sound in approach. Provisions are under way to observe a group of patients utilizing ATA as a chelating agent in the hope of producing a better drug than those now available in the management of this very difficult disease.

In summary, it might be said that with our greater knowledge of the epidemiology and toxicology of beryllium, we can to a great measure prevent the occurrence of this fatal disease by proper medical engineering controls.

Unfortunately, at this stage of our knowledge we can offer the patient with chronic beryllosis only early diagnosis by annual x-ray surveys of exposed populations. Upon diagnosis it remains a matter of continued supportive therapy along with the judicious use of cortisone or ACTH and the promise of fruitful research in the field of the chelating agents.

Transvaginal Pelvioscopy (Peritoneoscopy)

A SIMPLIFIED AND SAFE TECHNIC AS AN OFFICE PROCEDURE

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THE differential diagnosis of an intrapelvic lesion or new growth that cannot be too easily delineated is a problem which frequently confronts the physician. Furthermore evaluation of ovarian function in the various menstrual disorders as well as that of tubo-ovarian function in infertility may require more definite elucidation. For these and other indications adequate direct visualization of the pelvic organs would indeed be a desideratum in helping to solve the problem. (Table 1.)

Transvaginal pelvioscopy (T.V.P.)* offers a simple means of accomplishing this. The purpose of this report is to present several modifications of Decker's original technic[1] which were developed to render it a relatively simple and thoroughly safe office procedure.[2,3] Decker pointed out the essential importance of the knee-chest position in order to simplify the direct observation of the tubes, ovaries, corpus uteri and adjacent viscera.[4] The instruments and equipment were adapted from those used in transabdominal peritoneoscopy.[5] The essential modifications of Decker's technic consist of: (1) The use of a holding device or support (Fig. 1) for the patient's legs so that she can remain stable as well as comfortable in the knee-chest position. (2) Introduction of 150 to 200 cc. of CO_2 gas to negate the intra-abdominal negative pressure, thus preventing air from being drawn into the abdominal cavity on withdrawal of the trocar. As a result, prolonged shoulder pains (from nitrogen) will be avoided. (3) The utilization of adequate but short-acting analgesic and sedative agents. (4) Proper psychosomatic orientation of the woman as to the procedure so that the fear-tension-pain syndrome may be minimized or prevented.

* The term transvaginal pelvioscopy has been adopted for several reasons. First, it explains the route used and the type of study made by it, while "culdoscopy" implies study of the cul-de-sac rather than that of the pelvic organs. Secondly, our Spanish-speaking colleagues prefer to avoid the term "culdoscopy" for esthetic reasons.

TABLE 1
INDICATIONS FOR TRANSVAGINAL PERITONEOSCOPY IN 400 CASES

Group	Indications	Total No. of Cases
Primary infertility	1. No pregnancy after a year of therapy 2. Repeated abnormal kymograph on tubal insufflation 3. Suspicion of previous pelvic infection 4. Previous laparotomy 5. Previous hysterosalpingography especially with oily medium 6. Irregular cycles; poor diphasic basal body temperature curves	196
Secondary infertility	Same as above	54
Secondary amenorrhea or prolonged cycles	Correlation of gross ovarian status with other data, to determine prognosis as well as therapeutic modality of choice	39
Ectopic pregnancy	Confirmation of diagnosis before laparotomy	21
Diagnostic	1. Differential diagnosis: ovarian cyst, myoma uteri, possible malignancy, postoperative adhesions 2. Clarification of pelvi pain	90

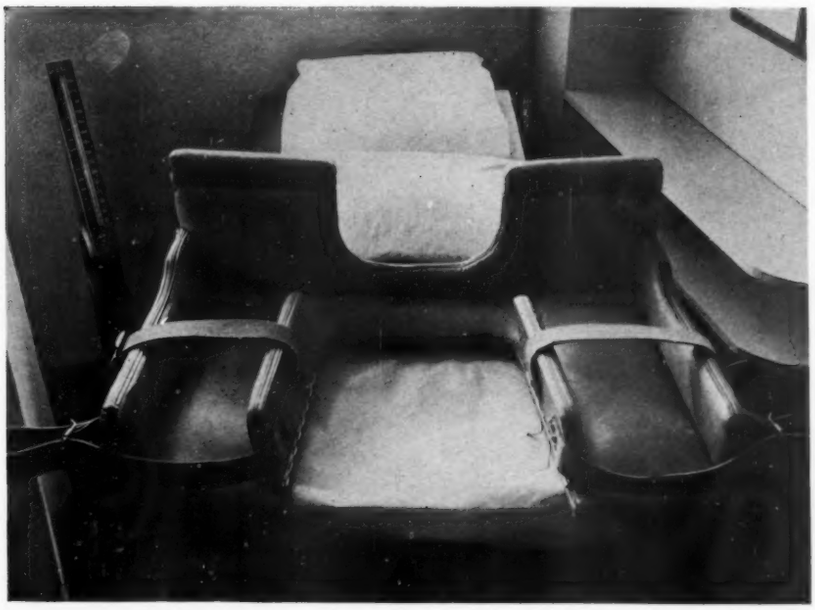

FIG. 1. Supporting device in place at end of ordinary examining table. The thighs and knees rest squarely against the upright portions, while the straps at the other end are then tightened very snugly around the instep of the foot. (Preferably, the patient should wear her shoes.) The strap in the middle is then tightened about the calf. The patient rests her breasts upon the first pillow, while her head is placed upon the second pillow (at the far end of the table). When comfortable, she is asked to arch her back inwardly in exaggerated lordosis. (This supportins stand is also very useful for proctoscopy.)

TECHNIC OF TRANSVAGINAL PELVIOSCOPY

The necessary equipment for transvaginal pelvioscopy, listed in order of use, is as follows: supporting stand (Fig. 1);* self-induction mask containing 10 to 15 cc. of trichlorethylene;† Sims' speculum, three sizes; cervical tenaculum (Braun), 7.5 inches; uterine packing forceps (Bozeman), 9.5 inches; 2 by 2 sterile gauze squares; aqueous antiseptic (zephiran® 1:1000 dilution);‡ 10 cc. syringe (Luer-Lok);§ spinal needle, 4 inches long, 21 gauge (Pitkin);§ procaine hydrochloride, 1 per cent solution; sheath and trocar (Fig. 4);** CO_2 gas, tubal insufflation apparatus;†† sliding air seal lock;** observation telescopes: (1) culdoscope,** (2) coellioscope (Gulbring 6 mm.);‡‡ rotating swivel contact (ACMI rotating contact);** connecting cord (ACMI);** battery with rheostat (ACMI);** uterine sound; uterine cannula, self-retaining (Jarcho);§ methylene blue solution 1 per cent in saline, sterile; 4 by 4 sterile gauze. (Fig. 2.)

The procedure will be described in detail as it is a relatively new one that merits more widespread use.

Orientation of Patients. First, the purpose of the procedure of directly visualizing the ovaries, tubes and uterus should be carefully explained to the patient and, if possible, to her husband in simple language that can be easily understood. Pictures are indeed very helpful. We have found a recent Ciba Symposia issue[6] of great help. The patient who understands the "why" of each procedure is the one who will cooperate completely.

It is pointed out that there may be at most three or four items of discomfort, all minor in degree (the word "pain" should be avoided completely). In any event, it should be emphasized that sufficient analgesia will be utilized

* A more modern, better upholstered one is now being made by Cottage Woodcraft, Los Angeles, Calif.

† An excellent apparatus is distributed by either Ayerst, McKenna and Harrison, Ltd., New York, N. Y., or Ohio Chemical and Surgical Equipment Co., Madison, Wis.

‡ Manufactured by Winthrop-Stearns, Inc., New York, N. Y.

§ Becton & Dickinson, Rutherford, N. J.

** Manufactured by American Cystoscope Makers, Inc., New York, N. Y.

†† Manufactured by Grafex Instrument Co., New York, N. Y.

‡‡ Manufactured by A. Guerin, Paris, France.

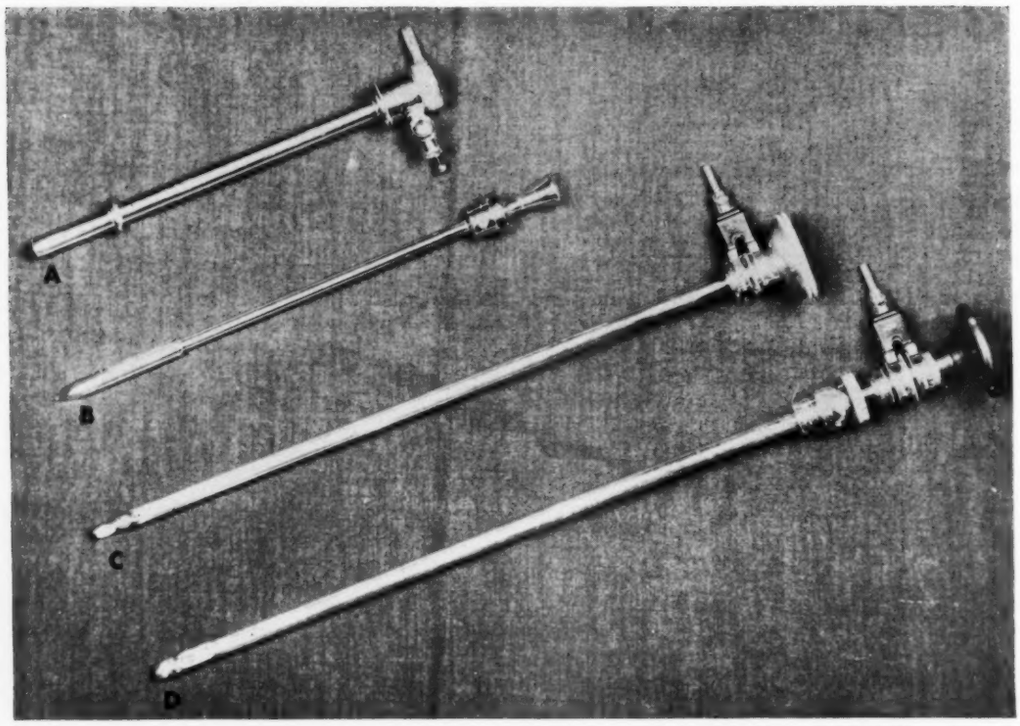

FIG. 2. Essential instruments for transvaginal pelvioscopy. A, sheath into which the grooved trocar (B) is locked prior to insertion through the posterior vaginal fornix into the cul-de-sac of Douglas. At one side is the two-way stopcock to permit entrance of CO_2 gas. C, the "coellioscope" of Palmer for observation of a 120° angle visual field. Note knob indicating direction in which lens is pointed. D, "culdoscope" of Decker for visualization of 90° angle. Note sliding air seal lock which fits into the sheath (A) and can be tightly locked in place. Just forward of the knobbed eyepiece is the swivel contact which can be coupled to a cord connected to a battery so as to light up the bulb at the other end.

to try to prevent any discomfort whatsoever. Most women are embarrassed by the knee-chest position. After explaining the reasons for this posture (increased negative intra-abdominal pressure plus the falling away of the intestines from the field of vision), the woman is assured that the room will be darkened with only a spotlight in the vagina. The second possible source of discomfort may be the pin-prick or transient burning sensation felt on introduction of the local anesthetic (procaine) into the posterior vaginal fornix. A third factor that may frequently be uncomfortable is the introduction of the trocar and sheath, although it is almost always transitory. Occasionally, if the CO_2 gas is introduced too rapidly, some momentary distress may occur. The woman is also assured that she will be told about each step before it is carried out.

Preoperative Preparation. On the morning of the pelvioscopy the patient is instructed to have a bowel movement or take an enema. A light breakfast such as juice, coffee and toast is permitted. It is suggested that someone come with her, preferably her husband, to take her home, since she may become dizzy or somewhat wobbly on her feet from the medications used to help her feel relaxed and comfortable.

When she appears at the office she is first advised to empty her bladder. Then, after removing all her clothes except her shoes, she puts on a loose-fitting gown that is open in back. For sedation she is given 50 to 100 mg. of secobarbital or sodium pentobarbital orally, as well as 50 to 100 mg. of either dramamine® (dimenhydrinate) or benadryl® (diphenhydramine hydrochloride), since they seem to have a synergistic effect. The room is darkened and she is told to close her eyes and relax a while. If the doctor or nurse stays with her, conversation in a soft, quiet tone about various non-medical subjects will markedly allay the patient's apprehension regarding this "new" procedure for which she so often secretly feels she is a "guinea pig."

Positioning Patient. When she feels somewhat drowsy or light-headed, the patient is

asked to "stand" on her knees so that the supporting device pictured in Figure 1 may be put into position. First, the right knee is placed in the proper angle snugly against the upright piece; then a strap is tightened, first about the instep of her shoe and secondly, about the right leg. The same procedure is carried out on the left side. While this is going on the patient should rest on her hands in a "crawling" position. After she is strapped in place, she is asked to place her breasts on the first pillow and her face on the second one (Fig. 3), arching her back in exaggerated lordosis while her hands rest limply at her side or under her head. At this point a self-induction apparatus containing 15 cc. of trichlorethylene is strapped to her wrist, and the mask placed against her face. She is instructed to take a few breaths at first and then to inhale deeply whenever she feels any discomfort. The use of meperidine hydrochloride (demerol®) has been discontinued because of the many undesirable side effects. Dilute sodium pentothal, if indicated, may be safely used in this position.

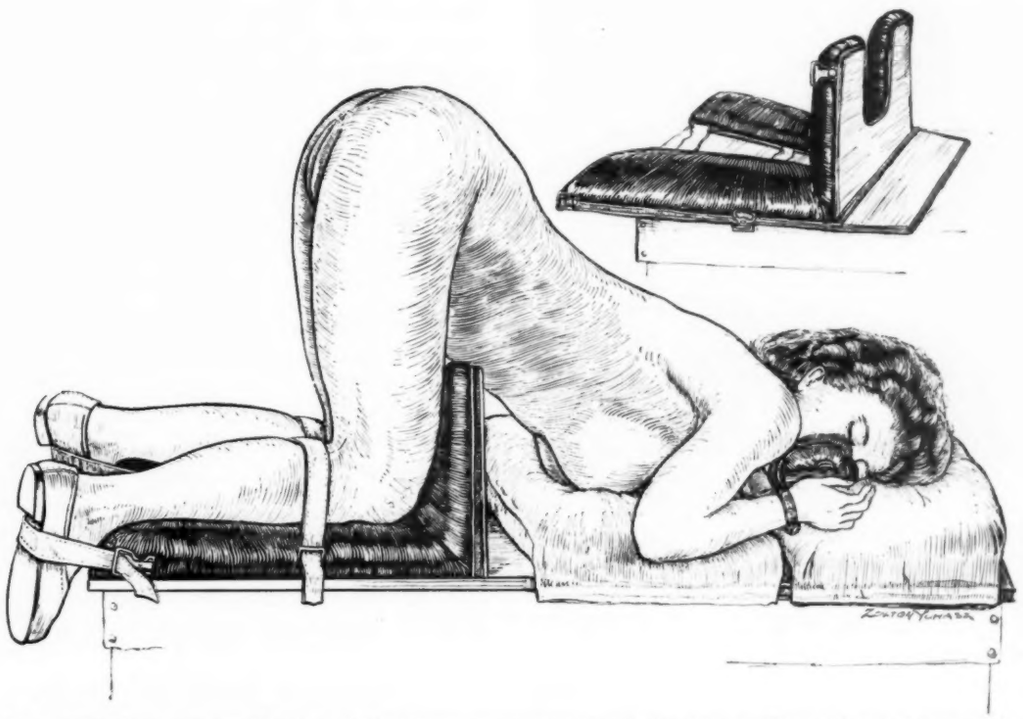

FIG. 3. Patient strapped into position. Note exaggerated lordosis of back. The self-induction mask containing trichlorethylene is strapped to the wrist.

Preparation of Instruments. The pelvioscope is sterilized by first washing the instrument with soap and cold water, rinsing it clean and then immersing it in one-tenth of 1 per cent (0.001%), that is, a 1:1000 dilution of aqueous zephiran® (alkyl-dimenthyl-benzyl-ammonium chloride) or similar substance for twenty minutes. "Anti-rust" tablets containing sodium nitrite should not be used in this solution as the cement about the lenses may be loosened sufficiently to permit moisture to enter and fog up the observation lens. All the other instruments may be "cold" sterilized in the same kind of solution, with or without the "anti-rust" chemicals. Before their actual use the instruments should be placed on sterile towels in a proper container and be permitted to dry completely. On the other hand, except for the observation telescope, all instruments may be sterilized by heat.

Insertion of Pelviscope. As each step is begun the patient is informed as to what she may expect. When she is fairly comfortable, a single Sims speculum, the size depending on the depth of the vagina, is introduced vaginally. With gentle traction the posterior vaginal wall is elevated up and anteriorly with the distal portion of the speculum retracting the bowel at a higher level than at the fourchette. The posterior lip of the cervix, which is now anterior, is grasped with a tenaculum. The vaginal

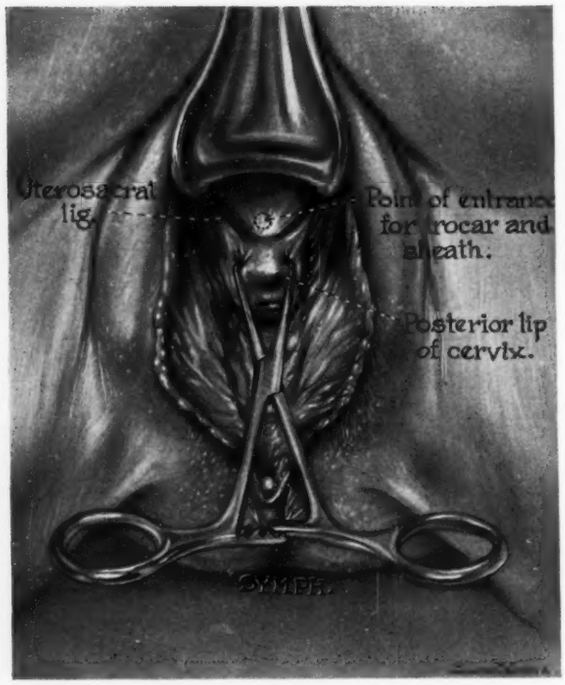

FIG. 4. The posterior vaginal fornix over the cul-de-sac hollowed out by firm downward pressure with the uterine packing forceps between the uterosacral ligaments.

vault is thoroughly swabbed with a detergent type of antiseptic, such as 0.001 per cent of aqueous zephiran.

With firm downward and somewhat forward traction on the posterior lip of the cervix, the converging folds of the uterosacral ligaments may be made to stand out. The empty uterine packing forceps, with its point downward, is slid forward on the cervix until it presses deep into the concave hollow between the uterosacral ligaments at a point about 2 to 3 cm. above their uterine insertion. Steady pressure will leave a somewhat blanched, rounded mark and at the same time hollow out still further the posterior fornix over the cul-de-sac area. (Fig. 4.) The patient is warned to inhale slowly and deeply from the mask if she feels some pressure or discomfort during this maneuver. With a long spinal needle (20 or 21 gauge) attached to a 5 cc. syringe, 2 to 4 cc. of 1 per cent procaine hydrochloride, without epinephrine, is infiltrated into the area about the mark left by the uterine dressing forceps. The patient should be skin-tested to procaine previously as this step may be omitted. The patient is advised that she may feel a slight sticking or burning sensation.

After a few minutes the patient is told that she may next experience a momentary pressing or sticking sensation. The vaginal membrane over the cul-de-sac is made taut from above by the Sims speculum, while downward and slight forward traction on the cervical tenaculum stretches it tight in the other direction. With the trocar locked in the sheath (Fig. 4), the point is pressed into the center of the infiltrated area. With a slight twisting motion the trocar and sheath are thrust inward gently but firmly through the mucosa and peritoneum in a direction parallel to the fundus. As they enter the peritoneal cavity, a sudden lack of resistance or "give" is usually felt.

If the site of the puncture is too close to the cervix, the retrocervical areolar space will be entered instead of the cul-de-sac. The same may occur if the vaginal membrane of the posterior fornix is not held taut. When this happens only a maze of areolar tissue will be observed. If the bowel is entered, the folds of rectal mucosa or feces will be seen. To test whether the cul-de-sac has been entered, the obturator may be loosened and gently withdrawn about 4 cm. until an in-sucking, hissing noise is heard. With experience this will neither be necessary nor advisable, as sufficient air may enter to cause "shoulder" pain for several days, since nitrogen is absorbed very slowly.

A very simple device to determine if the peritoneal cavity has been entered is to attach a U-tube to the two-way stopcock on the sheath. The U-tube should be very narrow in diameter, about 2 to 4 mm., and half-filled with dilute methylene blue. After the stopcock is turned, the level of the blue fluid will drop in the outer arm of the U-tube and rise in the inner arm, if the peritoneal cavity has been successfully entered. The drop is caused by the negative intra-abdominal pressure.

Pneumoperitoneum with Co_2. If the pneumoperitoneum is made with air, the nitrogen in the latter is absorbed so slowly that shoulder pain on assuming the upright position may persist for many days. As a result, a most uncomfortable and bitterly complaining patient will literally haunt the doctor. Carbon dioxide, however, is absorbed in a matter of minutes. As an alternative oxygen may be used.

With the obturator and sheath in place the CO_2 insufflation apparatus, preferably with a volume and pressure measuring device, is connected by a rubber tube with a male tip to the two-way stopcock valve on the side of the cannula. The stopcock is turned so as to

permit 150 to 200 cc. of CO_2 gas to pass slowly into the abdominal cavity. Very little head pressure is necessary as the negative intra-abdominal pressure will draw the gas in. (In our experience the Kiddie-Decker CO_2 apparatus, designed to perform this, has proven to be of very little help.) The obturator has a small groove along one side (the latest models have three such grooves) to permit the gas to pass easily. The patient usually notes a sensation of bubbling of gas in the abdomen. While the sheath is held steady in position, the obturator is withdrawn. As a rule a small amount of gas can be heard "whooshing" out of the sheath. An observation telescope is introduced through the sheath and locked in position. It is connected to dry cell batteries (capacity 4 volts) with a rheostat to regulate the amount of light. The room is darkened.

When the pelvic viscera are clearly visualized, the Sims speculum should be removed to allow for greater freedom of motion of the observation telescope. A small metal knob is present at one point at the periphery of the eyepiece to indicate in what direction the lens is pointed.

As a rule the right angle pelvioscope (culdoscope) is adequate for securing an over-all "bird's eye" view of the pelvic organs. For greater ease of manipulation as well as for realizing a clearer, more sharply defined picture, the coellioscope with its 120 degree visual field and somewhat brighter bulb light has proven superior in many ways. On the other hand the sheath, swivel contact, sliding air seal lock and connecting wire that go with the culdoscope set, are much more functional than the same accessories that go with the coellioscope. However, the experience of the individual operator must determine what instruments work best in his hands.

The Pelvic Survey. The pelvis is systematically surveyed; first the corpus, then the adnexa and finally the adjacent viscera. By means of gentle pressure on the anterior abdominal wall with the one hand, combined with manipulation of either a tenaculum on the cervix or with a uterine sound pressing within the uterine cavity, visualization is usually complete. In addition, one may determine patency of both tubes by inserting a self-retaining uterine cannula (Jarcho) and then slowly injecting through it from 5 to 10 cc. of 1 per cent methylene blue solution in normal saline. By observing the fimbriated end of the tube, patency of that tube may easily be established.

Postpelvioscopic Care. When the examination is completed the telescope is removed. With one hand pressing firmly over the region of the umbilicus, as much gas as possible is expressed through the open sheath before the latter, as well as the tenaculum, are removed. A ball of cotton or gauze is placed snugly in the introitus. After the straps are loosened with the patient in "crawling" position, the knees are brought to the midline and the holding device removed. The patient's right hip is placed on a pillow so that her hip rests at a higher level than her head.

In about thirty to fifty minutes the patient will usually be able to arise and get dressed. If acute shoulder pain develops, she is advised to lie on her right side with the hip elevated. In a few cases this may last for twenty-four to seventy-two hours (especially if some air entered the abdominal cavity), although in the great majority, shoulder pain on arising will either be minimal or absent in one to twelve hours. In some 25 per cent of the cases lower abdominal aching or discomfort may be present. As a rule 30 mg. (0.5 gr.) of codeine phosphate combined with 650 mg. (10 gr.) of aspirin is sufficient to render the patient comfortable. No douching or intercourse is permitted for at least three days. The puncture site is then inspected. If it is still oozing, a hemostatic, such as Monsell's solution (basic ferric sulfate solution) may be applied. In any event, sexual relations should be deferred until the puncture site is healed.

Complications. To date, no really serious complications have followed pelvioscopy. In over 400 such procedures, the bowel has been entered five times, an incidence of just 1 per cent. Expectant treatment alone was used with every case making an uneventful recovery. In each instance the patient was extremely tense and relaxation was not complete. For such women it is now preferred to carry out pelvioscopy under dilute sodium pentothal.

In two cases low grade pelvic cellulitis developed following intercourse the day after pelvioscopy. With antibiotics the infections were rapidly brought under control. Profuse vaginal bleeding from the site of entrance of the trocar, after intercourse, occurred in one patient six days after the procedure. This flow was controlled with vaginal packing. Finally, one woman developed mild muscle twitching because of sensitivity to procaine.

By far the most common side reaction has been nausea or an uneasy "queazy" feeling in the epigastric region following the use of meperidine. As a rule this is transitory. The other common side reactions have been shoulder pain or lower abdominal discomfort lasting for no more than two or three days.

It should be mentioned in passing that several patients have been pelvioscoped two, three and even four times.

Failures. In eighteen instances pelvioscopy was unsuccessful on the first attempt. Seven women were so poorly oriented psychosomatically that the procedure had to be stopped before or during the introduction of the trocar and sheath. Pelvioscopy was successfully carried out under sodium pentothal in five, while two refused.

In five women the bowel was inadvertently entered on the first attempt. Since the point of entrance in the bowel is retroperitoneal, the danger of peritonitis is absent. Simple judicious, watchful waiting was all that was necessary. The patient should be warned that occasionally rectal bleeding may occur, but not to worry about it. There were no other complications in these women. As a matter of record, four of them underwent a second attempt successfully.

In three cases early in this series, only the retrocervical areolar space was entered, causing the observation telescope to slide behind the peritoneal membrane. All three were successfully done on the second attempt.

In two cases the bulb burned out; and since a spare one was not available, these were listed as failures.

In one case mild convulsions followed as a reaction to procaine hydrochloride. Under sodium pentothal a successful result was obtained.

COMMENTS

From many viewpoints the value of transvaginal pelvioscopy as a diagnostic instrumentality of the highest import is clearly evident. Economically, the patient is spared the expense of hospitalization. Surgically, by pinpointing the diagnosis the physician is able to determine whether laparotomy is necessary, thus reducing considerably the number of operations for suspected gynecologic lesions. Actually, this procedure has been called "doing an exploratory laparotomy in the office." As a matter of fact, in a great number of the ninety cases listed under the diagnostic group, the question of surgery was resolved by the findings on transvaginal pelvioscopy.

Furthermore, in a group of twenty difficult diagnoses in which the patients were examined by three well qualified gynecologists, the correct diagnosis was arrived at in only 50 per cent of them before pelvioscopy.

As in all such procedures skill develops only with experience. It has been suggested that whenever the surgery schedule permits, each patient undergoing abdominal surgery for gynecologic reasons be pelvioscoped first, either in knee-chest position or in lithotomy in high Trendelenburg position. Findings should then be dictated or written down and later correlated with those found during laparotomy and with the report of the pathologist. In this manner one can easily learn to distinguish various phases of the development of the Graafian follicle, the early and mature corpus luteum, as well as the lesions of endometriosis, pelvic inflammatory disease, lipoid peritonitis, pelvic tuberculosis and others.

SUMMARY

A reasonably simple and thoroughly safe technic is described for carrying out transvaginal pelvioscopy as an office procedure.

Acknowledgment: The author gratefully acknowledges the aid rendered in many ways by his former associates, Dr. L. B. Anderman, Dr. D. I. Seibel and Dr. M. R. Osterman.

A 16 mm. color film of Transvaginal Pelvioscopy as outlined previously is available from Aron-Schon Productions, 684 S. Bonnie Brae, Los Angeles, 57, Calif.

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Simple Coupling Methods for Polyethylene Tubing

SIDNEY HIRSCH, M.D., *Cedarhurst, New York*

POLYETHYLENE tubing is being used more and more extensively in therapy and diagnosis. It has found a unique place in intravenous and intra-arterial therapy, and in caudal, spinal and epidural anesthesia.

Since the ends of polyethylene tubing will flare out when near a flame, many couplers have been designed and are available for the attachment of the tubing to Luer slip adapters.

The following are some simple methods for attaching the polyethylene tubing to most of the intravenous medications that are now commonly in use. These methods may easily be adapted to other needs as they present themselves.

Method 1. The plastic Luer slip adapter, as marketed with most of the intravenous sets, has an inner hole that gradually narrows near the smaller end. After the polyethylene tubing has been inserted in the vein and the needle used for insertion withdrawn, it is then threaded through the plastic adapter which is momentarily removed from the intravenous set. The outside end of the polyethylene tubing is held about ¼ inch away from a lighted match or alcohol flame and a flare developed by rotating the tubing gently. The plastic adapter is then pulled up on the tubing until the flare of the polyethylene tubing fits snugly, thus making its own gasket. The adapter is then reconnected to the intravenous set and is ready for use.

Method 2. If one does not wish to disconnect the plastic adapter from the intravenous set, a similar adapter may be used as previously described and the adapter in the set connected to the first adapter.

Method 3. Any female Luer slip hub may be easily separated from its shaft with a hacksaw. The small end hole in the hub is enlarged by using a 5/64 steel drill. After sterilization the hub is ready for threading with the polyethylene tubing as previously described.

Shoulder Pendulum Exerciser

LASZLO ORMANDY, M.D., *Washington, D. C.*

ANY intrinsic or extrinsic shoulder condition that produces prolonged immobilization of the shoulder joint will result in a frozen shoulder. The underlying cause is muscular inactivity which may be due to a fracture or dislocation in or about the shoulder joint with prolonged immobilization, acute or chronic subdeltoid bursitis, injury, bicipital tenosynovitis, operative procedures in or about the shoulder with prolonged immobilization and shoulder-hand syndrome following coronary occlusion. This disabling syndrome will produce pain and stiffness of the shoulder but can be avoided by proper shoulder exercises which should be started as soon as practical.

The shoulder exercises are well described in the textbooks with the exception of the basic exercise, which is the pendulum exercise. This exercise is usually done improperly because pain and spasm of the shoulder girdle muscles will splint the joint as a protective mechanism and the result will be that the patient will rotate his body or bend his elbow instead of creating motion in the scapulohumeral joint.

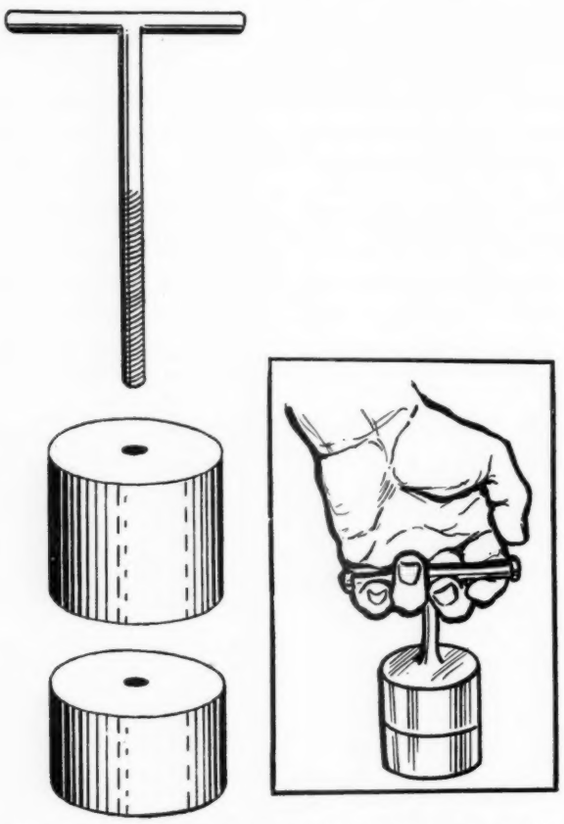
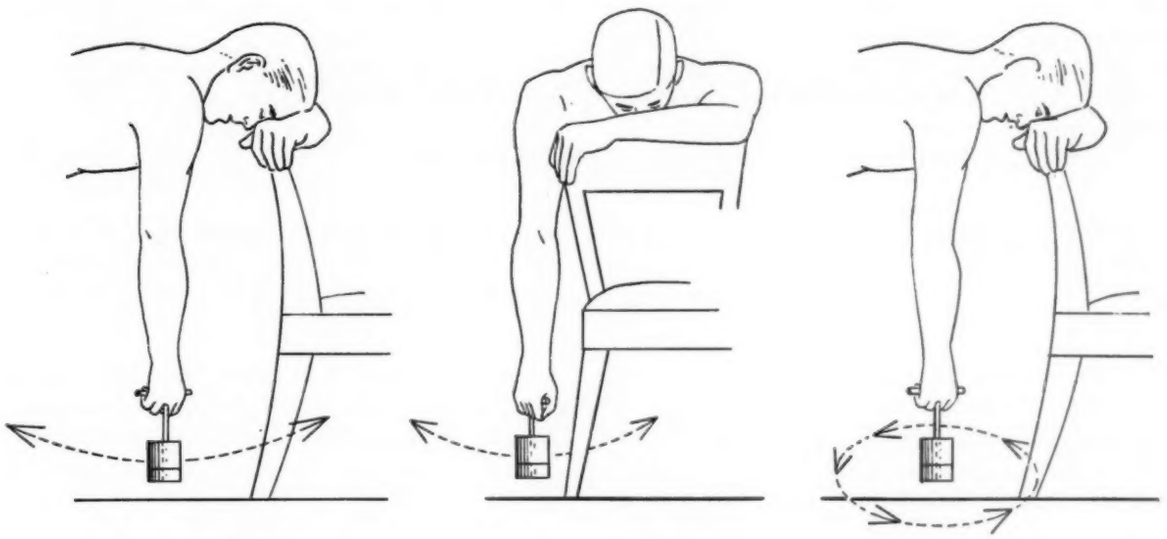


FIG. 1. Pendulum exerciser (weights: 3 plus 2 pounds). Inset: handle should be held loosely.

In order to perform the pendulum exercises properly the patient places the hand and forearm of the sound extremity on the back of a straight chair and stoops over, so that his forehead rests on his wrist, with the pendulum exerciser* held in the hand of the involved side.

* Manufactured by Bowen Company, Inc., Bethesda, Maryland.



2A 2B 2C

FIG. 2. A, sagittal plane; B, coronal plane; C, circumduction.

The exerciser consists of a T bar. On the vertical bar 5 pounds' weight (2 plus 3 pounds) can be threaded. (Fig. 1.) The horizontal bar is held by the semiflexed fingers. The handle should not be tightly grasped, but just held loosely. (Fig. 1, inset.)

The weight of the exerciser will produce traction thus relieving muscle spasm and pain, and also will stretch the contracted tissues. By swinging the exerciser in a sagittal and coronal plane, the arc of movement gradually will increase in the scapulohumeral joint; circumduction will be carried out also. (Fig. 2.)

The exercises should be done ten times in each plane about five times a day.

External and internal rotation can be carried out also while the arm is perpendicular to the ground and the upper extremity rotated externally and internally.

Reversed pendulum exercise will increase external rotation of the shoulder joint. This is done in the following manner: The patient is seated and rests the elbow of the involved extremity on a table. With the exerciser in the hand the patient carries out pendulum motion of the forearm in a coronal plane, that is, across the chest. (Fig. 3.)

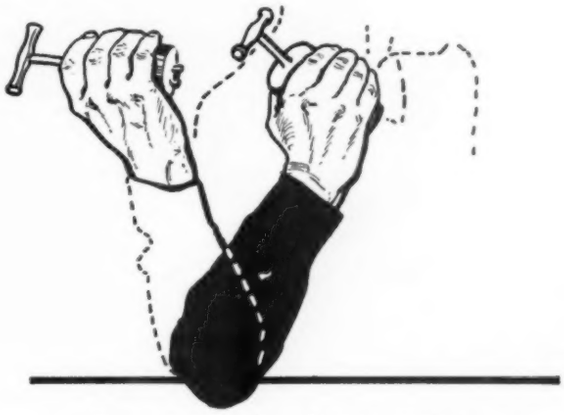


FIG. 3. Reversed pendulum exercise.

Beside this basic exercise all other routine exercises should be added according to the progress of the patient.

SUMMARY

1. The importance of early pendulum exercises is stressed in conditions in or about the shoulder.

2. A pendulum exerciser is described which will relieve muscle spasm and pain while the patient performs shoulder pendulum exercises efficiently.

3. The compact size of the pendulum exerciser makes it possible to increase the arc of motion without hitting the leg of the patient.

An Important Diagnostic Aid in Rectal Examination

THE VALUE OF STRAINING IN THE SQUATTING POSITION

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THE squatting position is rarely used as part of the examination of the rectum and anus. Bacon[1] devotes only a few lines to its use in his textbook. He states that "In palpating proc-

1 2

FIG. 1. Anal examination with the patient in the knee-chest position. One external hemorrhoid is seen.

FIG. 2. By squatting and straining prolapsing of internal hemorrhoids and marked external hemorrhoidal engorgement are seen, demonstrating the value of this procedure.

identia and polypoid growths it is sometimes helpful to have the patient assume the squatting position." For the past few years, as part of the routine rectal examination, we have made it a practice to have the patient strain in this position. The information thus obtained has been impressive.

Rectal discomfort and hemorrhoids are the cause of many patient visits to the physician. The problem of recommending either conservative or surgical treatment is presented. Often the patient's complaints are minimized and the examiner is unimpressed when the routine rectal examination is conducted with the patient in the knee-chest or lateral Sims position. The venous channels are emptied since the blood is drained from the vicinity of the anus. However, when the patient is placed in the squatting position and asked to strain, much more information is obtained because the situation simulates that which occurs at defecation. The gravity effect of a column of blood is present which is further accentuated by the patient's straining. Blood is forced into the terminal hemorrhoidal veins by the increased intra-abdominal pressure caused by the contraction of the diaphragm and the voluntary abdominoperineal muscles. Prolapsed internal hemorrhoids, procidentia and weakness of the perineal musculature are easily demonstrated by these maneuvers.

A routine digital, anoscopic or proctoscopic examination is first made. The importance of the procedure to follow is then explained to the patient. The doctor's assistant has the patient stand on the knee support of a Buie table and assume the squatting position by straddling the edges of the table. He is then asked to

strain or "bear down." If a Buie table is not available, a chair or stool can be used for the test. This additional examination requires only a few more minutes and is time well spent in the evaluation of the rectal disease. An illustration of the merits of this procedure can be seen in Figures 1 and 2.

In summary, this supplemental maneuver should be performed in order to evaluate and complete a survey on every patient with rectal complaints. It will not only demonstrate prolapsing internal hemorrhoids, procidentia and weakness of the perineal muscles, but also will show the presence of marked external hemorrhoidal engorgement not visualized by other methods. This examination will definitely aid the physician in recommending appropriate therapy, conservative or surgical.

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Review of a series of almost 2,000 consecutive thyroidectomies showed a 7 per cent incidence of primary malignancy. The nodular goiters operated upon showed an incidence of primary cancer amounting almost to 10 per cent. Postoperative recurrence most frequently happens in cases in which the cervical lymph nodes were found involved in the primary operation. Only in cases with frank lymph node involvement is radical neck dissection needed, and then only when there is no evidence of distant metastases. In view of these statistics it is not surprising that practitioners recommend prompt surgery in instances of nodular goiter. (*Richard A. Leonardo, M.D.*)

Surgical Management of Unusual Anorectal Lesions

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SURGICAL removal of the rectum can be accomplished in a number of ways, and many different types of operations have been described. In general, these operations can be divided into two classes: those that preserve the anal sphincter and those that do not.

The Miles abdominoperineal resection is of course the most widely used of all those operations that remove the anal sphincter and is the standard operation for carcinoma of the rectum. The Lockhart-Mummery procedure, which consists of perineal resection of the rectum following preliminary sigmoid colostomy, is occasionally used in elderly or debilitated patients. The Lahey two-stage operation and the perineo-abdominal resection are simply modifications of the Miles operation and are useful under some circumstances. The Kraske resection, which leaves the patient with perineal or sacral colostomy, is of historical interest only and has no place in modern surgery.

Sphincter-saving operations are less commonly used, especially in carcinoma of the rectum. It is a moot question whether any sphincter-saving operation satisfies the criteria for radical resection of malignant disease of the rectum. The surgical literature contains a great many articles setting forth the pros and cons of this argument. It is not within the scope of this brief presentation to discuss these points.

Anterior resection and direct anastomosis can be accomplished at a level within a few inches of the anus. However, the use of this procedure in all but the highest rectal lesions is open to serious criticism.

Abdominal resection and perineal anastomosis has certain advantages in that the anastomosis can be carried out more easily and under better vision. One operation of this type, the so-called "pull through" operation, has achieved popularity recently, especially in high rectal lesions and in certain benign conditions such as Hirschsprung's disease.

Finally, perineal resection and anastomosis, the Cuneo operation, has been used by some surgeons but has not become popular in this country because it affords limited removal of the gland-bearing areas involved.

The following cases are presented because of their unusual nature and because they demonstrate the use of a few of the more common methods of resection of the rectum.

CASE REPORTS

Colloid Carcinoma of the Rectum with Perforation

CASE 1. A forty-six year old housewife was admitted to the hospital in November, 1950. She complained of pain in the rectum which had begun two weeks previously and had gradually increased in severity until on admission the pain was constant and agonizing. For several days before admission the patient had had difficulty with both defecation and urination. There had been no subjective chills or fever. There was no history of bowel disturbance prior to the present illness except for long-standing constipation. Ten years previously a large ischiorectal abscess had been drained. The past history was otherwise negative.

The general physical examination was normal. Temperature was 100°F.; there was deep tenderness in the perianal area but no redness or swelling. The patient refused to allow rectal examination because of extreme tenderness. Vaginal examination revealed marked tenderness and induration in the region of the rectum.

FIG. 1. Photomicrograph showing carcinoma invading perirectal connective tissue. Note acinar structures filled with mucinous material.

On admission the white blood count was 12,600, and the urine showed numerous red blood cells.

A diagnosis of high ischiorectal or pelvirectal abscess was made, and the patient was taken to the operating room for examination under anesthesia. Rectal examination revealed an orange-sized mass in the presacral space. During the course of the examination the mass ruptured into the rectum, discharging a large amount of yellowish, gelatinous material. A biopsy was taken from the rectal wall in the area, and the cavity was counterdrained through the skin anterior to the coccyx. The biopsy showed well differentiated colloid carcinoma arising from the rectum. (Fig. 1.)

It was thought that radical resection of the rectum and perirectal tissue offered the only hope of arresting the growth; however, routine abdominoperineal resection would almost certainly spread viable tumor cells into the peritoneal cavity. An extraperitoneal resection through a perineal approach, namely, the Lockhart-Mummery operation, seemed the best solution to the problem.

Accordingly, as soon as the diagnosis of carcinoma was confirmed a left lower quadrant, double-barrel colostomy was established. One week later resection of the rectum was performed with the patient in the prone position. Through a midline incision the coccyx and last two segments of the sacrum were excised. The rectum, together with the anus, levator muscles and perirectal tissue, was resected as high as the peritoneal floor. The proximal rectal stump was closed.

The postoperative recovery was uneventful. Approximately one month after the operation the patient received x-ray treatments in the amount of 7,600 r.

In the twenty-seven months since operation the patient has continued to do well except for pain in the region of the posterior incision. This had been a persistent problem. In the past five months severe sciatic pain developed which has been incapacitating. On a recent examination there was, however, no evidence of local or distant recurrence of the growth, and the neurologic examination was negative. X-rays of the spine and pelvis showed no metastases. In spite of this negative evidence we believe it is likely that there is tumor present to account for the nerve root type of pain. The patient has been seen by a neurosurgeon who advised and performed prefrontal lobotomy for relief of pain. Since that time the patient has continued in apparent good health,

FIG. 2. Typical malignant ulcer involving perianal skin. Medial edge of tumor obscures the anal opening.

with little pain and no demonstrable recurrence of the tumor.

Squamous Cell Carcinoma of the Anus

CASE II. A thirty-nine year old man was sent for consultation because of a "tumor in the anal area." Approximately one year previously the patient noticed a small nodule near the anal opening. The nodule became irritated during hot weather. The lesion ulcerated about five months before admission and has continued to weep since. There had been progressive, slow growth of the tumor, but the patient kept hoping the lesion would disappear. He was finally seen and sent in by his family physician. The past history was negative except that the patient had had pruritus ani for a number of years.

The physical examination was essentially negative except for the anal area where a typical malignant ulcer, measuring 6 cm. in diameter, was located on the right side at the anal verge. (Fig. 2.)

A biopsy was taken and proved to be squamous cell carcinoma. Abdominoperineal resection was performed with wide removal of perianal skin. The immediate postoperative course was complicated by pulmonary atelectasis and fascial disruption from which the patient recovered promptly.

The resected specimen showed no metastases to the perirectal lymph nodes.

After a few weeks at home the patient was returned to the hospital and a one-stage, bilateral, inguinofemoral lymph node dissection was performed. Of the lymph nodes thus removed, one showed a solitary metastatic tumor implant. Wound healing of both femoral incisions was delayed because of serum accumulation beneath the skin flaps.

One year postoperatively the patient continued to be in good health except for slight swelling of the upper thighs, scrotum and penis, which is gradually receding. There has been no recurrence.

Epithelioma of the anus is not a particularly rare condition, and the treatment is well standardized. The end results are, as a rule, less favorable than adenocarcinoma of the rectum, and the chief site of spread is the inguinofemoral lymph nodes. The only aspect of the disease to be discussed herein is the sequence in which the two stages of the surgical treatment are performed. Most surgeons advise removal of the primary growth first with resection of the inguinal nodes at a second stage. This is in accordance with the surgical principle of controlling the primary tumor before attacking the area of metastases. In epithelioma of the anus there is much to be said for reversing this procedure.

Wound healing in groin dissection is notoriously poor, particularly after colostomy has been established in the left lower quadrant. Furthermore, a large superficially infected perineal wound draining by way of the lymphatics into the inguinal nodes further increases the chances of wound infection. In the next case to be presented the groin dissection was performed before resection of the rectum, and both femoral wounds healed without infection.

Malignant Melanoma of Anus

CASE III. A sixty year old farmer was first seen because of rectal bleeding. During the previous two months the patient had noticed frequent appearance of bright red blood in the stools. There was also dull aching pain in the rectum, which was not especially influenced by defecation. After examination by his family physician the patient was referred to our care.

The general physical examination was essentially negative.

Proctoscopic examination revealed an irregular, nodular growth involving the entire circumference of the anal canal at the mucocutaneous border. A diagnosis of squamous cell carcinoma was made and the patient was admitted to the hospital.

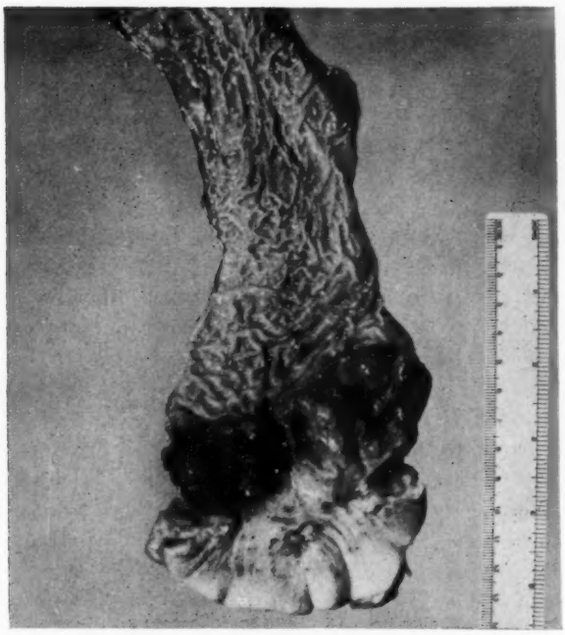

FIG. 3. Malignant melanoma almost encircling anus at mucocutaneous border. Note similarity in appearance of this lesion and thrombosed hemorrhoid.

Biopsy revealed malignant melanoma. Abdominoperineal resection and bilateral groin dissection were planned, and in this case it was elected to perform the groin dissection first. This was done on both sides simultaneously using two surgical teams. Both wounds healed *per primam*. The specimens removed contained thirty-one lymph nodes in all, none of which contained tumor. (Fig. 3.)

Ten days following this operation abdominoperineal resection of the rectum was performed. Metastases were found in five of twelve lymph nodes removed with the rectum.

Recovery from this operation was uneventful, and the patient was discharged after two weeks. He did well at home for about three months, then suddenly began complaining of headaches and showed signs of confusion and disorientation.

On readmission to the hospital it was noted that the patient's condition had obviously deteriorated. There was marked mental clouding and confusion. The margins of the optic discs were blurred, but the neurologic examination was otherwise negative. There was a questionable mass in the region of the liver, but no signs of perineal recurrence. X-ray of the chest was negative. A presumptive diagnosis of cerebral metastases was made. The patient rapidly became unmanageable so that it was necessary to transfer him to a mental hospital for care. His death occurred within a few weeks and autopsy was not performed.

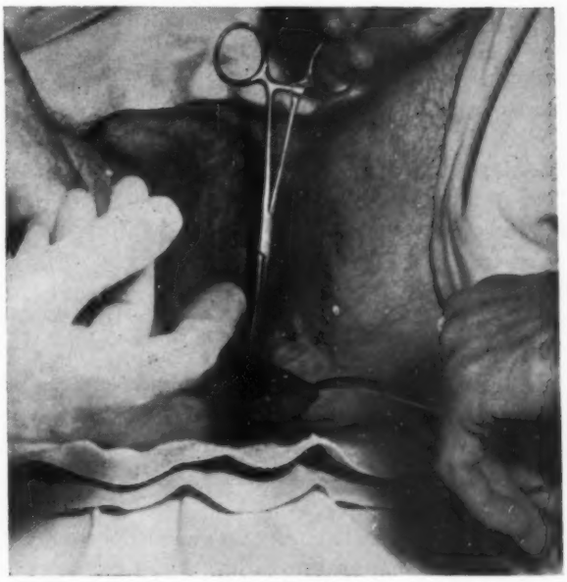

FIG. 4. Necrotic, prolapsed, tubular membrane representing the entire rectal mucosa.

Malignant melanoma of the anus is quite rare. In 1944 Bacon[1] collected all cases reported in the literature up to that time and found only eighty-five authenticated cases of anorectal melanosarcoma.

Several authors have commented on the similarity in appearance of darkly pigmented melanomas and thrombotic hemorrhoids and have pointed out the necessity of careful pathologic examination of all tissue removed at the time of hemorrhoidectomy.

The results of treatment of malignant melanoma are, as in this case, uniformly poor. Radical surgery seems advisable only because there is nothing else to offer the patient.

Stenosis of the Entire Rectum

CASE IV. A forty-two year old farmer was admitted to the hospital with the following unusual history:

Approximately six weeks before admission the patient had been operated upon for nasal polyps. While convalescing, he spent a day mending the floor in his barn. Two weeks following this he was admitted to his local hospital with classic signs and symptoms of tetanus. The disease was relatively mild, and he recovered promptly under the usual treatment for that condition. Some form of medica-

tion (possibly paraldehyde), which the patient said was "too hot to drink," was given by rectum for the purpose of sedation. There was burning pain in the rectum for a short while thereafter. The patient required numerous enemas for relief of constipation, and after one of these enemas a strand of tissue prolapsed from the rectum. At this point the patient was transferred to our care.

Physical examination revealed the patient to be in good general condition. There was some residual muscle spasm particularly in the facial and abdominal muscles. There was moderate tympanitic distention of the abdomen. Protruding from the rectum was a strand of necrotic tissue which appeared to represent the entire rectal mucosa. (Fig. 4.)

After a short period of observation a double-barrel colostomy was established in the transverse colon. Recovery was rapid, and the patient was discharged from the hospital to be followed as an outpatient. During the ensuing months there was gradual and progressive stenosis of the entire rectum until the lumen was almost completely obliterated. Only a small amount of water could be forced through from the distal colostomy opening.

The patient continued in good health and carried on the usual duties of a farmer. One year after his original hospitalization he was readmitted for further treatment. It was decided to attempt resection of the stenotic rectum and reconstruct the bowel.

The first phase of the operation was done through a left rectus incision. There were numerous pelvic adhesions. The sigmoid and upper rectum were mobilized, a suitable length of sigmoid was moved into the pelvis, and the peritoneal floor was closed above it. After closure of the abdominal wound the patient was shifted to the prone position with the legs flexed.

A midline posterior incision was made, through which the coccyx and lower two sacral segments were removed. There was dense fibrosis of all pelvic structures, and the rectum was mobilized with considerable difficulty. It was found to be completely stenotic to within ¾ inch of the mucocutaneous border. After it was freed the rectum was resected and the sigmoid anastomosed with a single row of sutures to the short cuff remaining at the pectinate line.

Recovery from this operation was uncomplicated; the wound healed by primary intention and the patient was discharged after two weeks.

The patient did well at home for several weeks, but returned after a month with signs and symptoms of low-grade small bowel obstruction. A barium enema examination revealed the anosigmoidal anastomosis to be patent. The small bowel obstruction persisted, and three days after admission exploratory laparotomy was performed. The peritoneal cavity, which a month before had seemed normal except for pelvic adhesions, was almost completely covered with whitish, inflamed-looking nodules. Entry into the peritoneal cavity was difficult because the small bowel was so matted together and fused to the parietal peritoneum. After biopsy of one of the nodules the wound was closed. The tissue removed showed adenocarcinoma.

The patient went downhill rapidly and died three weeks later. Autopsy showed extensive diffuse carcinosis arising from linitis plastica involving the distal third of the stomach.

This tumor of the stomach was undoubtedly present at the previous operation, although it was certainly not evident through the lower abdominal incision. Re-examination of the tissue removed at the previous operation showed several small tumor implants lying between the muscular layers of the rectum. Apparently the pelvic operation scattered tumor cells widely or in some way stimulated such rapid dissemination of the growth.

SUMMARY

Four cases of unusual anorectal lesions are presented and discussed. Because of their unusual nature, each was a special problem in treatment, and the surgical management illustrates some of the less commonly used methods of resection of the rectum.

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Neurilemmoma of the Sigmoid Colon, Associated with Diverticulitis As a Cause of Obstruction

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NEURILEMMOMA is a benign specific nerve sheath tumor and is composed of Schwann's cells, which in a sheath constitute the inner cellular covering of nerves. It is an encapsulated, firm, fibrillar tumor of the nerves of the extremities and viscera. Many names for this tumor have been suggested, including neurilemmoma, neurinoma, schwannoma, peripheral glioma, perineural fibroma, neurofibroma and peripheral fibroblastoma.

Stout has divided the benign tumors of nerve sheaths into two distinct types, that is, neurilemmoma and neurofibroma. Neurofibroma is unencapsulated, having a tangled network showing schwannian sheath proliferation. Special stains show large numbers of neurits. This type of tumor may undergo malignant change. The neurilemmoma is encapsulated and is made up of Antoni type A and Antoni type B tissue. Antoni type A tissue is composed of bands of cells with their nuclei arranged in parallel order. Antoni type B tissue is made up of cystic spaces containing gelatinous-like material. According to Murray, both of these tissues are specific and can be grown in tissue culture. Neurits are seen only in the compressed capsule. This tumor is non-malignant but it may recur locally.

There is evidence that the Schwann cell sheath, which constitutes the inner cellular covering of peripheral nerve fibers, is a neural crest derivative like the leptomeninges.

The location of these tumors is varied. No mention was noted in the literature of neurilemmoma in the intestinal tract. Intracranial and intraspinal neurilemmomas arise most often in the auditory nerve, especially in its vestibular branch, and in the posterior roots of spinal nerves. They may occur on any other cranial nerve except the olfactory and optic cranial nerves. They make up about 10 per cent of intracranial tumors, and almost one-third of intraspinal tumors. These tumors have been reported in the posterior mediastinum, usually discovered on routine chest x-ray examination. Gross reported a neurilemmoma of the humerus, and Hicks and Warren report them as being found in large tumor formations in the mediastinum, abdominal cavity and extremities. Ackerman states that he has seen two neurilemmomas involving the tongue and several neurofibromas arising in the pharynx. He mentions that the fine radicles of the facial nerve can be the origin of neurilemmoma, and this can be present in the region of the parotid salivary gland. Both neurilemmoma and neurofibroma have been associated with generalized von Recklinghausen's disease, but the neurilemmoma may be seen without such manifestations. The neurilemmomas occur most commonly on the flexor surfaces of the extremities.

The neurofibroma may become malignant and, according to Ackerman, the preferred name of this tumor then is neurofibrosarcoma. The early malignant changes in a neurofibroma are very difficult to detect and may consist only of slightly increased cellularity with beginning prominence of the nodule. There is a tendency to have local recurrences before distant metastases occur.

The differential diagnosis of neurilemmoma of the sigmoid colon would include the benign tumors such as neurofibroma, singly or associated with von Recklinghausen's disease, fibroma, myxoma, lipoma, hemangioma, leiomyoma, endometrioma in females, etc., and the malignant tumors such as neurofibrosarcoma, sarcoma, lymphoma, carcinoma, argentaffinoma, hemangioendothelioma, hemangiosarcoma, etc. Lymphosarcoma is the most common form of sarcoma of the intestinal tract. Hemangiosarcoma is a malignant proliferation of both fibroblastic connective tissue and vascular tissue. Hemangioendotheliomas result

from malignant proliferation of endothelial cells. Ganglioneuroma is usually benign and arises from ganglion cells of the sympathetic nervous system. Perithelioma, usually of low grade malignancy, arises from perithelium, the connective tissue accompanying capillaries and smaller vessels.

CASE REPORT

A. W. S., a fifty-three year old white man, was examined on September 21, 1954. At that time he complained of lower abdominal pain, especially in the right lower quadrant, and difficulty in passing bowel movements of two months' duration. His condition had become progressively worse and he had vomited on the previous day. Bowel movements had become progressively less voluminous but more frequent, about three to six being noted per day. Some mucus had been noted in the stools but no blood had been seen.

Past history revealed that the patient had been operated upon for an apparent ruptured appendix with abscess formation at the age of sixteen. The appendiceal abscess was drained and later the appendix was removed.

Examination revealed a thin, slightly pale, middle-aged man. His blood pressure was 100/60. The abdomen was moderately distended. Just medial to the lower aspect of a lower right rectus incision scar marked tenderness was noted. Some tenderness was noted deep in the left lower quadrant of the abdomen. The prostate gland was normal to palpation.

Laboratory work revealed the urine to be entirely normal, and the complete blood counts and sedimentation rates to be within normal limits.

The sigmoidoscope was passed to 14 cm. Further passing of the sigmoidoscope was limited by fixation of the bowel at that area. Some mucus and blood were noted on the mucous membrane of the bowel. At the level of 12 cm. a small polyp was found, which was removed. The pathologic diagnosis of this tissue was benign polypoid adenoma.

The barium enema studies were rather difficult to complete. The barium flowed into the rectum, then hesitated at the rectosigmoid area. With a little slow steady pressure and kneading, the barium eventually passed this area and then readily filled the colon. A Bardex bag inflated in the rectum was of some value in the further study of this rectosigmoid area. Numerous diverticula, ranging in size from ½ by ½ to 1 by 1 cm., were noted in the sigmoid area. There appeared to be marked kinking of the colon at the rectosigmoid area. Evacuation was slow and fairly complete. X-ray of the lungs revealed no abnormalities.

The patient was hospitalized for one week and then treated at home by conservative methods in an effort to determine if a benign inflammatory lesion was present causing obstructive symptoms which would respond to a non-residue diet, sulfasuxidine® and terramycin.® The treatment was continued for three weeks and barium enema studies were repeated. It was possible to pass the sigmoidoscope for 2 or 3 cm. further, but here the passage was limited again by fixation of the colon. Barium enema studies revealed little or no change, with obstruction of the rectosigmoid area still rather marked.

The patient was admitted to the hospital again for elective surgery to relieve the colonic obstruction. At surgery the following findings were noted:

The small intestine appeared to be moderately acutely inflamed. There were dense adhesions between loops of the small bowel and between the small bowel and the anterior abdominal wall in the right lower quadrant, secondary to previous surgery for appendiceal abscess. There was a marked inflammatory reaction and adherence between a loop of the ileum and the sigmoid secondary to diverticulitis of the sigmoid. An indurated area, whitish in color, was present on the small intestine at the site of adherence to the sigmoid. The sigmoid colon was redundant, kinked on itself, and was markedly adherent to the surrounding parietal peritoneum deep in the pelvis; the adhesions caused a kink in the rectosigmoid area. There was evidence of an acute recent inflammatory diverticulitis. Moderate inflammatory reaction was still present.

A lower left rectus incision with splitting of the rectus muscle was made. The adhesions between the small bowel and the sigmoid were separated by blunt and sharp dissection. A biopsy was taken from the wall of the ileum at the site of the attachment to the sigmoid. This area of the ileum presented a hard white substance imbedded in the wall. The report of the frozen section was inflammatory reaction,

no malignancy. The defect in the intestinal wall was closed. Adhesions between loops of the small intestine and between the small intestine and the anterior abdominal wall in the right lower quadrant were separated. The sigmoid colon was further separated from adherent structures by blunt and sharp dissection, and the area was located for resection containing an acute inflammatory process and several diverticula. The elected site of resection was prepared for anastomosis. A segment of sigmoid colon about 7 inches long was resected. The omentum was placed over the operative site and the wound was closed in layers. A small Penrose drain was placed on top of the closed rectus fascia and brought out in the inferior aspect of the wound.

The pathologic report revealed the following: Part one was a resected portion of the sigmoid which actually measured 9.5 cm. in length and varied from 2.5 to 3.5 cm. in width. Attached to it was a small amount of yellow lobular fat, part of the fat being appendices epiploicae. The structure contained a small amount of brownish fecal material; the mucosa was soft and rugose throughout, presenting no evidence of tumors. On the exterior of the structure, however, most of it appeared to be covered by fairly smooth-appearing greyish pink serosa. One area was present, however, that was ovoid, measuring up to 3.5 by 2.5 cm. in diameter which lay upon the lateral surface of the structure; when sectioned it appeared to be an abscess involving the fatty tissue and underlying tissue with what appeared to be fatty necrosis. This was not reflected within the wall as one cut through the tumor. Representative sections of this and of the other portions of the structure were taken for histologic study.

An additional piece of tissue was taken from the serosal covering of the ileum. This measured .5 by .7 cm. and was taken also wholly for sections and study.

Histologic examination revealed the following: Several sections of the tissue were removed. First seen were sections of the bowel wall itself including the mucosa immediately over the area of tumefaction that was described in the outer portion of the bowel. The mucosa appeared to be entirely intact; the lymphoid follicles were not markedly increased in size. The musculature appeared normal and there was no evidence of tumor. In the outer structure, however, including the serosa and subserosal connective tissue, a considerable degree of inflammatory reaction was seen and the actual swelling that was observed appeared to be composed of a frank neoplasm that was made up of cells which were spindle to ovoid in shape. In some instances they retained a polarity that was quite remarkable, strands and strings of cells passing along together with nuclei that tended to be slightly wavy. It was therefore believed that this had risen from some neurogenic structure within the subserosal connective tissue of the bowel wall. Superimposed upon it had been a fair amount of chronic inflammatory reaction which lately had become more acute, there being basically a tremendous number of lymphocytes and some hemorrhage, and superficially a fair number of polymorphonuclear leukocytes and some tissue necrosis. In a careful search through the tumor cells they were seen to be made up of wavy bands and bundles of cells with very little stroma between them although they appeared to be of the connective tissue type. Trabeculae were not frequent among the tumor cells. The cells appeared fairly uniform in size, shape and staining reaction, only a fair number of them being exceedingly hyperchromatic. Mitotic divisions were not seen and evidences of invasion of the bowel wall were not observed. The tumor therefore was benign. In some instances tendencies toward palisading of cells were seen and occasional poorly formed giant cells were observed. The inflammatory reaction appeared non-specific.

Seen also were sections of the biopsy removed from the ileum. It was made up of connective tissue within which there were considerable amounts of inflammatory reaction. The pattern was non-specific. *Diagnosis:* Neurilemmoma, subserosal tissue, of colon; chronic ileitis, focal.

The postoperative treatment consisted of continuous Wangensteen suction to combat distention, intravenous glucose with electrolytes and antibiotics consisting of penicillin with streptomycin.

The postoperative course was markedly uneventful. The first two postoperative days the patient had a temperature of 1 to 1½ degrees elevation. On the third postoperative day he had a loose bowel movement. The bowel movements were loose for the next two days and there were three to four movements daily. They then became of more normal consistency,

and the patient has had one to three movements daily since the operation.

Postoperatively the patient immediately began to improve generally. He gained 10 pounds in the first month postoperatively, and one month after surgery he returned to his normal occupation.

Barium enema examination taken six weeks after operation still showed some hesitancy for the barium to pass the rectosigmoid area, apparently due to some spasm of the colon in this area; however, the barium did fill and distend the large bowel well. No evidence of any local constriction of the bowel was seen, and evacuation was quite complete in six hours.

Sigmoidoscopic examinations seven weeks postoperatively revealed moderate fixation of the sigmoid colon above 17 cm., but good visualization was permitted to 22 cm. No abnormalities were seen.

COMMENTS

A case of neurilemmoma of the sigmoid colon associated with diverticulitis causing obstruction has been presented. This is a rare tumor and is infrequently found in the intestinal tract. It is important to differentiate the nerve sheath tumors, consisting of neurilemmoma and neurofibroma, because although the neurilemmoma is entirely a benign tumor, neurofibroma may become malignant. It is often difficult to designate whether or not a neurofibroma is malignant. There is a tendency for repeated local recurrence of neurofibroma before there is evidence of distant metastases. There is also a tendency with each recurrence to have increasing microscopic evidence of malignancy.

Neurilemmomas may be associated with von Recklinghausen's disease (multiple neurofibromatosis) and they may be associated with neurofibromas undergoing malignant change; hence neurilemmoma, neurofibroma and neurofibrosarcoma may exist in the same area.

The treatment of neurilemmoma is surgical. While mere removal of the tumor renders a cure, the diagnosis is made by microscopic examination of the tissue. Therefore wide excision is advisable since one has to distinguish between this tumor and neurofibroma or neurofibrosarcoma. Where it is difficult to perform a wide excision, frozen section examination of removed tissue may be suggested as an aid in establishing the minimal limits of excision. However, in this type of tumor such a procedure may not prove practical because of the difficulty in determining evidence of malignancy, particularly if there has been some degenerative changes such as mucoid degeneration, necrosis, hemorrhage and cyst formation.

In this case the relationship of neurilemmoma to diverticulitis would be the same as the relation of neurilemmoma to a chronic inflammatory process elsewhere in the body. The relationship here is believed to be coincidental and the usual treatment was directed for the handling of lower large bowel obstruction. Since neurilemmoma was diagnosed and not neurofibroma, no plan of observation for the recurrence of this tumor has been instigated, merely the usual follow-up observation for a postoperative case of diverticulitis.

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Intraperitoneal Perforation of Infected Urachal Cyst

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PATENT urachus and urachal cyst, while not rare entities in infancy, are infrequently found in adults. In a review of the literature up to 1952 Sterling and Goldsmith[1] were able to collect only twenty-eight proved cases of urachal tract disease in which the symptoms and signs appeared after the age of five years. Urachal anomalies are susceptible to infection, but intraperitoneal perforation is an extremely rare complication. In only one of twenty-eight cases collected by Sterling and Goldsmith did this complication develop (originally reported by Everett[2]). Tauber and Bloom[3] reported the case of a two and a half year old boy with perforation of an infected urachal cyst which simulated an appendiceal abscess.

CASE REPORT

A twenty-one year old white man (HRN 30 532) was admitted on June 6, 1952, because of severe abdominal pain. His illness had begun insidiously with the development of mild periumbilical discomfort five days before admission. On the following day he noted a small amount of dark, foul-smelling umbilical discharge. The symptoms continued with the same intensity until the night before admission when he experienced an acute episode of severe abdominal pain, followed by intermittent crampy lower abdominal pain. He became anorexic but did not vomit. Bowel movements were normal.

Four months earlier he had experienced periumbilical pain associated with a "sticky" bloody umbilical discharge. Hygienic care resulted in prompt subsidence of his symptoms.

Pertinent findings on physical examination were limited to the abdomen. A dirty purulent exudate was observed to emerge from an edematous, inflamed umbilicus. A small concretion of inspissated debris was removed from the umbilical pouch. Both tenderness and rebound were present over an area 5 cm. in diameter around the umbilicus. Tenderness was most marked in the midline inferiorly. No mass was palpable. The abdomen was not distended and bowel sounds were normal. Rectal examination revealed tenderness high in the midline, referred to the anterior abdominal wall as well. His temperature was 100.2°F., his pulse 80 and his blood pressure 124/80. White blood count was 12,500 with 86 per cent

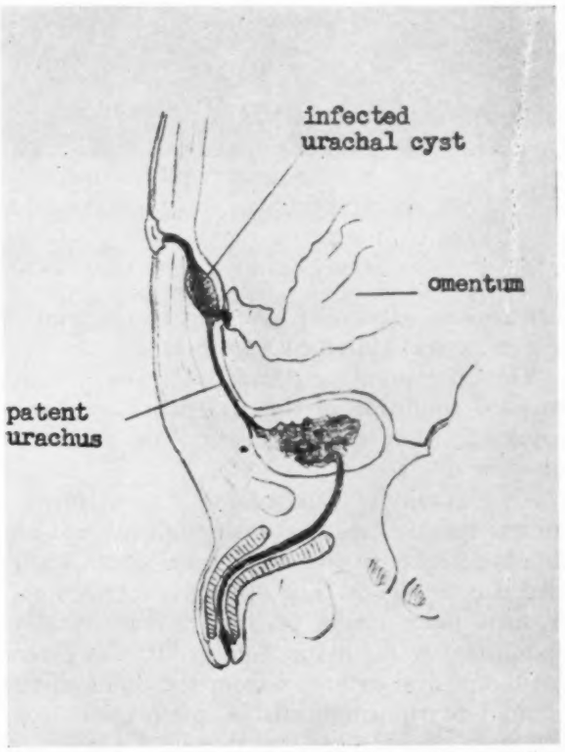

FIG. 1. Diagrammatic sagittal view of operative findings.

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FIG. 2. Dissection of umbilicus with urachal tract in extraperitoneal stratum.

FIG. 3. Probe passing from external umbilical sinus through cyst into patent urachus.

neutrophils. Urinalysis and roentgenograms of the chest and abdomen were normal.

The preoperative diagnosis was "acute surgical condition of the abdomen," probably resulting from a complication of persistent vitelline duct.

An exploratory laparotomy was performed under spinal anesthesia through a mid-abdominal right transverse incision which encircled the umbilicus. The appendix was normal. A firm mass could be felt in the anterior abdominal wall, in the midline. It was extraperitoneal and extended from the dome of the bladder to the umbilicus. A perforation from the mass into the peritoneal cavity was sealed by attachment of indurated and hemorrhagic greater omentum. (Fig. 1.) While freeing the omentum, a small amount of odoriferous purulent material emerged from the point of perforation. A pure culture of Staphylococcus aureus was grown from this exudate. A cord-like structure was dissected inferiorly from the umbilicus to the dome of the bladder in the extraperitoneal stratum. (Fig. 2.) The tract was divided at the bladder and the distal end transfixed.

A probe was passed from an external umbilical sinus through the infected cyst into the patent urachus. (Fig. 3.) A point of rupture was present at the junction of the urachal cyst with the tract. Microscopic examination revealed a cornified squamous epithelium lining the cyst, with marked infiltration by neutrophils and round cells.

The patient was discharged to duty after a ten-day uneventful postoperative course. He was entirely well when examined twenty-two months later and had had no untoward symptoms.

COMMENTS

The presence of persistent or recurrent drainage from the umbilicus most commonly results from omphalitis, an anomaly of the urachal tract, or an anomaly of the omphalomesenteric duct. The presence of genitourinary complaints and the character of the drainage material will frequently suggest the diagnosis: Clear fluid with genitourinary complaints is indicative of a patent urachal tract; fecal material strongly indicates bowel communication; and purulent discharge without genitourinary complaints, a local inflammatory process. Radiographic visualization of dye injected into an umbilical sinus, cystoscopy and cystogram when indicated will usually establish the diagnosis.

Failure to investigate adequately the underlying cause for persistent umbilical drainage may result in the development of complications such as closed-space infection, bladder infection or peritonitis from perforation.

SUMMARY

1. A patient with an acute abdominal syndrome caused by the intraperitoneal perforation of an infected urachal cyst is reported.

2. Adequate early investigation of persistent or recurrent umbilical discharge is stressed.

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Kistner and Smith studied the effects of routine administration of dicumarol in a very large series of cases of major surgery performed on women over the past five to ten years, and found that the incidence of postoperative thromoembolism was considerably reduced, probably by this prophylactic therapy. These patients usually received 100 to 200 mg. of dicumarol every fourth day during their hospital stay, starting with the night prior to surgery. The idea seems well worthy of further trials as no untoward results, except slight ones, occurred. There were no fatalities, hemorrhagic or otherwise. Recently dicumarol has been given in the average case without any laboratory control. (*Richard A. Leonardo, M.D.*)

Buschke-Loewenstein Tumors (Giant Condylomata Acuminata)

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IN 1896 Buschke[1] described a form of condylomata acuminata with the clinical, but not the histologic appearance of penile carcinoma.

Whereas Buschke was the first one to analyze the condition clearly, he was not the first one to observe and report it. In 1804 Martens and Tilesius[12] published an Atlas of Venereal Diseases. They show a picture (Fig. 17 of their article) which reminds one of the disease with which we are concerned. Ricord[15] in 1851 wrote a treatise on venereal diseases. In Figure 48 of his article he pictures what he describes in his own words as "vegetations frambésiées avec phimosis et perforation du prepuce." (The latter two sources were not available in original form and are quoted from Frei.) Ricord cautioned not to confuse these lesions with carcinoma. Considering the status of the diagnostic means at his command this was indeed a remarkable observation. For the same reason we should not hold it against the authors if they include the disease among those called "venereal."

In later years Buschke and his co-worker Loewenstein as well as Frei, Muehlpfordt and Treite wrote of this medical phenomenon.[2–4,13,14,16] In this country Gersh[6,7] devoted several publications to the same problem.

Clinically, one is dealing with a lesion of the following characteristics: inside a phimotic prepuce develops what looks like an ordinary condyloma acuminatum. Soon nodular areas of induration appear in the prepuce and later in the skin of the penile shaft, particularly in its dorsal aspect. Gradually perforations occur in the periphery of these nodules. Out of the resulting fistulas sprout new condylomas and putrid smelling pus. The fistulas merge and leave large holes in the skin of the penis and prepuce. Eventually the penis may more or less be grown over with condylomatous masses.

In an ordinary condyloma the strata are histologically well differentiated and the epithelial proliferation never goes beyond a certain depth. This is basically the structure of a so-called giant condyloma. The only important histologic as well as clinical distinction is the tendency to grow into deeper tissue layers. This growth in depth is, however, strictly one by expansion and not infiltration. Nevertheless, the tissue in front of the on-coming condyloma masses, particularly the corpora cavernosa, can be destroyed by compression.

There is always an area of "skirmishing" round cells to be found between the normal tissue and the condyloma. Although one may find a few epithelial pearls, there is no disorderly structure or growth, no invasion of lymph or blood vessels and no metastasis. Any lymph node enlargements are due to inflammation.

Certainly the destruction of tissue is a sign of malignancy but it is of utmost importance whether it is done by expansion or carcinomatous infiltration.

This problem has caused some confusion in the literature. The point in question clearly is whether or not these lesions are precancerous.

Freudenthal and Spitzer[5] talk about "condylomatoid precanceroses" and "condyloma-like carcinoma." Muehlpfordt[13] also uses the same expression. He argues that the histologic diagnosis should not be decisive and prefers what he calls the "much simpler and safer clinical conception of malignancy." He cites two cases, one of Israel[10] in which a truly precancerous condition existed. However, this clearly showed up in the microscopic slide. In the second case, the first biopsy showed condyloma and the second proved to be carcinoma of the frenulum. It is a basic rule that biopsies have to be extensive and there is always a possibility of the described carcinoma of the frenulum having been the primary lesion, causing the formation of secondary condylomas by its decomposition. The same can be said about the case reported by Herman.[9] No one can contest the fact that any fibroepithelioma, as a condyloma is, can occasionally

progress into a carcinoma. It is possible that in Muehlpfordt's case such a condition existed. He talks of Unna-Delbanco disease and actually describes an acanthoma which is something different than a condyloma acuminatum. The term "precancerous" cannot be used loosely. According to Borst and Meyer one would have to conceive that transformation of a certain tissue into carcinoma is the rule and not the exception. Treite had observed condylomata acuminata with several recurrences over a period of twelve years. Finally squamous cell carcinoma developed. Quoting the aforementioned thesis of Borst and Meyer, he still declined to call the primary lesion precancerous.

Etiologically no clear-cut explanation for the formation of condylomas has been advanced. There is the possibility of a filtrable virus. However, there is also no doubt that the moisture and irritation of the smegma in the preputial space is at least a strong supporting factor as Gersh has stressed.

TREATMENT

Radiation treatment has been tried without success. One may hesitate to use podophyllin in such an extensive lesion. Fulguration has been used and evidently was sufficient in some cases. Surgery is the treatment of choice. It may vary from local excision by knife or electroloop to amputation of the penis.

A comparatively large number of amputations of the penis are cited in the literature. Some cases are reported cured with less formidable methods. Frei, who reported five cases treated by fulguration, desiccation and circumcision, is the only author mentioning a plastic repair using scrotal skin. No argument shall be presented against amputation because it is extremely difficult to judge a case without having actually observed it. The large number of recurrences make it mandatory to remove all pathologic tissue in the first stage of any treatment.

We present our case because its outcome should encourage an attempt of radical, yet conservative treatment even in an advanced stage of the disease.

CASE REPORT

W. D. was a thirty year old, white, unmarried man. His family and personal history were non-contributory. Fifteen years prior to admission he had gonorrhea and was cured without sequelae. He was never circumcised and was perfectly well until about mid-October, 1950. He then observed that his penis began to swell and became hard around the edges of the prepuce. He was unable to pull his foreskin back and a slight discharge appeared. Soon he felt an indurated area on the dorsal portion of the shaft of the penis about in mid-length. He was treated with penicillin injections. On December 13, 1950 he was hospitalized because there was no response to treatment.

Physical examination was negative except for local findings. Blood pressure was 108/62. Temperature ranged between 98° and 99°F. during the whole period of hospitalization. Urinalysis revealed the following: pH 4.5, albumin negative, sugar negative. Microscopic examination showed a few white and red blood cells. Kline test was doubtful (repeat was negative). Sedimentation rate was 60 mm. in 60 minutes. Hemoglobin was 13.5 gm. per cent. White blood count was 10,500 with eosinophils 3 per cent, stab forms 2 per cent, segmental neutrophils 75 per cent, lymphocytes 15 per cent and monocytes 5 per cent.

The penis was swollen to three times its normal size and there was considerable edema. The urethral orifice was just visible in the ring of the much enlarged prepuce. The middle third of the penile shaft was very indurated but not tender and there were four areas of ulceration with a central depression and a peripheral corona of cauliflower type granulations, which readily bled. The largest one of these areas measured 2.5 by 2 cm. A foul-smelling white-yellow pus oozed from the prepuce and the perforations. The remaining skin of the shaft was very tight and there was bilateral, painless, inguinal adenopathy.

On December 13, 1950, a dorsal slit was done. The prepuce was found to be filled with condylomas. Biopsies were taken from the prepuce and the shaft tissue. Pathologic report indicated heavily inflamed loose connective tissue lined on one side by masses of papillary structures, with marked hyperplasia and hypertrophy of the Malpighian layers of covering squamous cell epithelium with acanthosis, mild parakeratosis and balloonization of cells. There were numerous bands of delicate connective tissue within the narrow stalks of papillae extending between the epithelial masses into the surface. In the stalks were round and mononuclear cells, sometimes perivascularly

FIG. 1. Photograph showing the condylomas of the preputial sac and the dorsal shaft perforation; the other ones being lateral are not visible. (P illustrates the perforation on the shaft.)

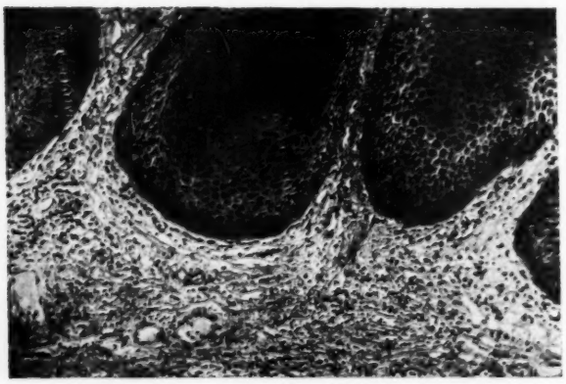

FIG. 2. Inflammatory reaction at base of condyloma.

arranged. In the grooves between the papillae much parakeratotic, sometime hyalinized matter and blood was found.

In the subepithelial spaces there was considerable round and mononuclear cell infiltration occasionally in perivascular arrangement, also enlargement of vascular spaces.

There was no invasion of epithelium into the underlying tissue. Occasionally, small granuloma-like structures were seen in the subepithelial connective tissue, consisting mainly of round, mononuclear and, rarely, giant cells of foreign body type.

Diagnosis was condyloma acuminatum of foreskin of penis with extensive papillary formations and acanthosis, occasionally perivascular arrangement of cells.

The patient was discharged on December 22, 1950. Treatment with antibiotics locally and by injection was continued.

The pathologic process progressed and he was seen by us on February 15, 1951. The description of the local lesion would be the same as the one on his first hospital admission, only that the areas of ulceration had enlarged and following the dorsal slit the glans was more visible. (Fig. 1.)

Clinical impression was penile carcinoma. The patient was hospitalized on February 19, 1951. General examination revealed nothing new. In general the laboratory findings were similar to the ones at first admission. On February 21st an extensive biopsy in depth was made; hemorrhage had to be controlled by fulguration. The specimen, 2 by 1.5 by 0.7 cm., was again diagnosed as "condyloma acuminatum." The first pathologist submitted it to another institution. The diagnosis was the same.

In spite of the wide extension we decided to try preservation of the penis but were convinced that we should sacrifice the larger portion of the skin and do a secondary plastic procedure. On February 24th the operation was performed under general anesthesia. After preparation and draping, a tourniquet was placed on the base of the penis. The skin was excised about 1½ cm. distance from the base to the glans. This included all the fungating masses. Laterally an incision was made at

FIG. 3. Stage 1 of plastic repair with bridge flap.

FIG. 4. Final result.

least ½ cm. into normal tissue. This left a narrow bridge of cutaneous covering over the corpus spongiosum. The fascial layer was removed and the corpora cavernosa were exposed. On one area, dorsally to the left of the midline, the condylomatous tissue had expanded into the corpus cavernosum. There we had to open and remove part of the corpus in order to be radical. Anteriorly the corona was sacrificed and on one spot a small portion of the glans, which otherwise was remarkably free of disease. All together 85 gm. of tissue was removed, the largest condylomatous area measuring 7 by 4 by 1 cm. (Pathologic diagnosis again was condyloma acuminatum.) (Fig. 2.)

The edges of the glans were fulgurated. The defect in the left corpus cavernosum was closed with lockstitch suture and the tourniquet removed. The larger vessels were clamped and tied. Other bleeding points were taken care of by suture ligation and fulguration. The skin on the lower surface as well as on the base was prevented from retracting by a few situating sutures.

The wound was treated with aureomycin ointment and the patient was placed on oral medication with the same drug, 250 mg. every six hours for ten days. He was discharged on February 28, 1951. After five weeks, the wound was clean, all catgut having been dissolved or absorbed, and there were healthy granulations with no signs of recurrence.

On April 3, 1951, he was hospitalized for stage 1 of the plastic repair operation which was performed on April 4th under general anesthesia. After preparation and draping, redundant granulations were removed from the penile wound. The skin edges on the dorsal portions of the glans and the base were freshened. A bridge flap about 5 cm. in width was formed from the anterior aspect of the left side of the scrotum, leaving both ends attached to the scrotal skin, but with sufficient clearance to accept the penis comfortably. The edges were attached to the glans and skin of the penile base. (Fig. 3.)

Again aureomycin dressings were applied and oral medication with the same drug was given. The patient was discharged on April 5, 1951. The flap took well.

In the subsequent admissions, first the left pillar of the bridge and later the right one was severed after test and the edges united with the small skin island on the lower surface of the penis, the glans as well as the skin of the penile base.

By August, 1951, the transplant began to thin out and the penis appeared fairly normal. Inguinal lymphadenopathy had subsided. (Fig. 4.)

Functionally there has been no complaint. The patient was married on December 25, 1951. He has been seen repeatedly since and to date there is no sign of recurrence.

COMMENTS

So-called giant condylomata acuminata "Buschke-Loewenstein tumors" are a rare variation of simple condylomata acuminata and, like these, generally originate in the preputial sac. Histologically they appear alike except for a pronounced front of round cell infiltration between the papillomatous structure and the normal tissue. Whether these round cells themselves play a role in the rapid expansion of these tumors or whether they are the expression of a yet unknown virus type

agent remains unknown. The tumors are easily mistaken for penile carcinoma because of their rapid growth and tendency to involve outside of the prepuce the whole shaft of the penis. A pure clinical conception of the disease has led to a certain confusion in nomenclature. The terms "giant condylomas" or "carcinoma-like condylomas" are perfectly in order. However, one must absolutely reject the classification of "condylomatoid precancerosis."

It must be kept in mind that the aggressiveness of these tumors is by expansion and penetration, not by infiltration as in the case of a carcinoma. The histologic diagnosis of proper biopsies must guide our plan of treatment. Because their growth is so rapid, we advocate early, radical yet preserving surgery, meaning removal of all involved skin into normal tissue (in width as well as in depth) even if it should involve partial re ection of the corpora cavernosa. Plastic procedures can follow as soon as the disease is controlled.

SUMMARY

A case of giant condylomata acuminata with extensive destruction of penile skin and expansion into one corpus cavernosum is presented. Radical removal of all diseased tissue into normal structures and secondary plastic procedure resulted in cure.

Pathology, nomenclature and treatment are discussed.

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An Unusual Urethral Fistula Site

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This paper describes a urethral fistula associated with bilateral removal of the ischium. This complication of spinal cord injuries has not been noted in the literature and has been observed in only two cases of approximately 1,000 at this center.

Case 1. Patient L. S. was injured on April 20, 1945. He sustained a complete spinal cord lesion below T10. The patient's condition was complicated by multiple bedsores requiring many operations including bilateral removal of the ischium. He had a well functioning neurogenic bladder.

The patient's last readmission was on October 7, 1952. Inspection showed a severe generalized edema. Over the medial edge of the ischium scar on the right a draining sinus was noted. Pressure over the site brought forth a copious amount of necrotic tissue. Laboratory observations revealed 12 gm. of protein in the twenty-four-hour urine specimen. The Congo red test showed amyloidosis.

A cystourethrogram was made which revealed a large diverticulum at the site of the previously resected ischial tuberosity. This was connected to the membranous urethra. Urethroscopy revealed a large opening on the right lateral aspect of the membranous urethra. The opening was large enough to admit a No. 24 panendoscope. Inspection of the diverticulum disclosed necrotic tissue hanging from the irregularly surfaced stump of the inferior pubic ramus.

A suprapubic cystostomy was performed on November 10, 1952. Although the patient was placed on his abdomen, the urine continued to drain from the ischial sinus. After treating the patient for hypoproteinemia edema, the urethra was severed with occlusion of the apex of the prostate through the perineum on September 30, 1953. Following the operation the edema increased and the condition became irreversible. Meanwhile, the ischial sinus stopped draining, but there was some drainage from the urethra. The patient's condition became worse and he died of amyloidosis on December 29, 1953.

Case 11. Patient J. G. was injured on December 21, 1947, and sustained a complete spinal cord lesion at T10. The patient's condition was complicated by multiple bedsores requiring many operations including bilateral removal of the ischium. He had a well functioning neurogenic bladder. A partial resection of the left ureter was performed because of an obstructing kink. Five days after the operation the inflamed kidney hemorrhaged severely which necessitated a nephrectomy of the left portion of the kidney.

The patient was readmitted because of a sinus tract at the medial portion of the previous right operative area. The Congo red test showed amyloidosis.

Cystourethrography indicated the condition to be the same as that in the previous case. (Fig. 1.) Upon urethroscopy the opening of the urethral fistula was noted at the same level as in Case 1, but was too small to admit the panendoscope.

Preoperative study revealed three kinks in the ureter; the lowest kink could not be passed by a catheter. Consequently, the method of choice for this patient was believed to be a cutaneous ureterostomy which was performed on March 19, 1954.

The ischial sinus stopped draining immediately and one week later the skin over the sinus tract was completely healed. A cystourethrogram was again taken which showed the disappearance of the diverticulum. (Fig. 2.)

COMMENTS

The fistula in Case 1 occurred nearly four and one-half years after a successful removal of the right ischium. In Case 11 it occurred two and one-fourth years after closure of the right ischial bedsore. Therefore, previous infection is not believed to be the cause of these fistulas.

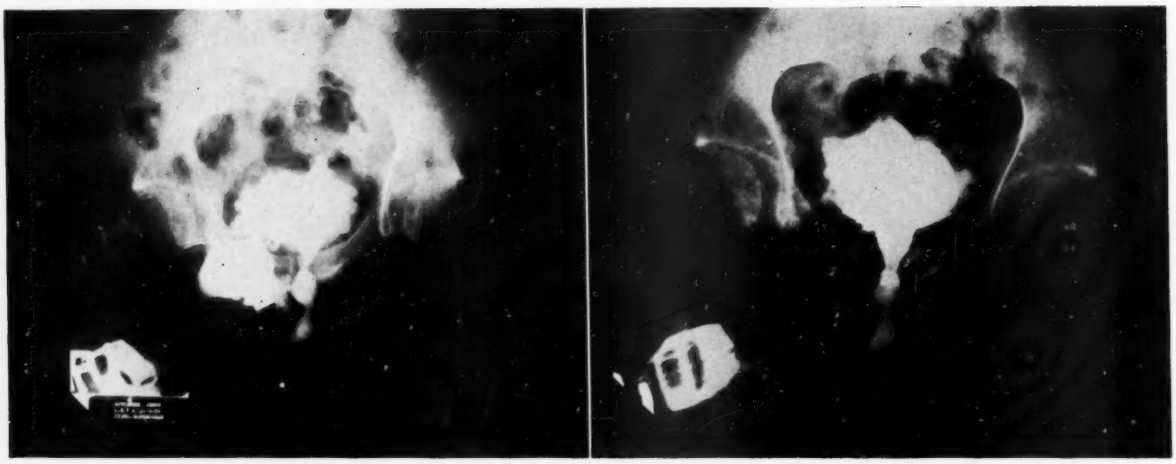

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FIG. 1. Cystourethrogram of patient J. G. Diverticulum is noted connected to the urethra. This diverticulum occupied the space of previous removal of the ischium.

FIG. 2. Diverticulum has disappeared following the cutaneous ureterostomy. Note the bilateral removal of the ischium.

The pathogenesis is as follows: Both patients underwent bilateral removal of the ischium. Subsequently, when sitting, the patient rested on the remaining bony prominence of the inferior pubic ramus. Persistent pressure produced a typical bedsore due to local ischemia, necrosis and infection. This infection probably spread through the two layers of the urogenital triangle or diaphragm which is normally attached to both ischiopubic rami but was detached during the previous removal of the ischia. The necrosis penetrated gradually through the surrounding tissue into the urethra.

It is interesting that both patients had amyloidosis. The amyloidosis was believed to be due primarily to the bedsores with bone involvement rather than to pathologic change of the urinary tract which was only the secondary cause.

Proper care of the skin may have prevented the ischial bedsores, removal of the ischia and would, in turn, have prevented the urethral fistulas.

Since this report was made, two other patients have been found with bilateral removal of the ischium.

SUMMARY

Two case studies of unusual urethral fistulas, complicated by bilateral removal of the ischium have been presented.

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Incomplete Cholecystogastric Fistula

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THE incidence of internal biliary fistulas is greater than is generally appreciated. The range of occurrence in patients with cholecystitis and in those undergoing biliary surgery is reported between 0.5 and 5 per cent. Reviews of autopsy series cite fewer instances of internal biliary fistulas.

Fistulous communication may occur between the gallbladder and any adjacent viscus, radicles of the biliary tree, or rarely the greater veins. The most common hollow viscus involved is the duodenum, and the least common, the stomach. Judd and Burden[1] included six biliary-gastric cases in a report of 153 internal biliary fistulas. Dean's review[2] of twenty-nine fistulas included only one with involvement of the stomach. In a group of 272 cases of biliary-enteric fistulas studied by Hicken and Coray[3] 4.4 per cent involved the stomach.

Symptoms usually accompany long-standing biliary tract disease. No particular symptom complex can be pathognomonic. However, an acute episode of abdominal distress followed by the appearance of calculi in stool or vomitus should clinch the diagnosis. The roentgenologic aspects have been reviewed extensively by Borman and Rigler, Hicken and Coray, Jenkinson and Lowry, and others.[3–7] Further review of the general features of internal biliary fistulas will not be made here.

This cholecystogastric fistula is reported because of the unusual way in which symptoms appeared. In addition, the manner by which such fistulas are formed is demonstrated in the following case.

CASE REPORT

This patient, a forty-nine year old white housewife, had had tarry stools for one week's duration four weeks previous to hospitalization. Subsequently increasing fatigue and weakness developed. Following an episode of black emesis, she consulted her physician who found her hemoglobin 8.5 gm., and referred her to the hospital.

For twelve years the patient had had "gallbladder attacks" which consisted of epigastric distress, intolerance to fatty foods, excessive eructation and an episode of jaundice ten years ago. Recent appetite had remained good and weight was maintained at 180 pounds. Bowel habit had been regular without recent change except for black stools. At no time had there been severe abdominal colic. Further past history and review of systems were non-contributory.

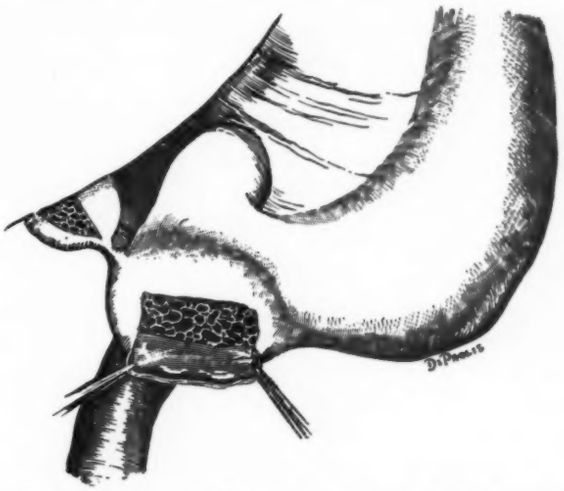

FIG. 1. Diagrammatic representation of the incomplete cholecystogastric fistula with intramural gastric pouch of gallstones.

Physical findings on admission included normal temperature, pulse, respirations and blood pressure. The patient was obese and slightly pale. There was mild epigastric and right upper abdominal quadrant tenderness but no palpable mass.

Hemoglobin was 10.2 gm. and hematocrit 30 vol. per cent. Leukocytes and smear were normal. Urine was negative. Non-protein nitrogen was 27 mg. per cent; prothrombin time, 100 per cent; blood sugar, 96 mg. per cent and glucose tolerance curve was normal. Serum amylase was 7 units; total serum bilirubin,

0.3 mg. per cent. Gastric analysis with histamine showed a response of 108 degrees free acid and 178 degrees total acid.

X-ray of the chest was negative. Cholecystogram showed no function of the gallbladder. Barium enema was normal. Gastrointestinal series demonstrated an extramucosal defect in the antrum of the stomach. On the lesser curvature side 5 cm. proximal to the pylorus, a mucosal erosion was visualized. The roentgenologist was of the opinion that an abnormal gallbladder with adhesions could explain the findings, although an extramucosal gastric tumor could not be ruled out.

After 1,000 cc. whole blood and forty-eight hours' bowel preparation with terramycin, the patient was operated upon on her tenth hospital day. Numerous dense adhesions were encountered. A globular mass 3 by 6 cm. containing numerous stones was palpated within the wall of the stomach. The gallbladder was freed and the stomach was opened above the mass. An exploring finger in the stomach and duodenum confirmed the intramural position of this mass. There was an hourglass constriction between this pouch of stones and the gallbladder. The gallbladder contained stones and was fibrotic. Cholecystectomy and choledochotomy was carried out with subtotal gastric resection. The pathologic report was chronic cholecystitis and cholelithiasis. The intramural sac of calculi in the stomach was lined with granulation tissue and covered by serosa and mucosa.

The patient's course was uneventful and she was discharged on her eleventh postoperative day. When seen three years later she was symptom-free.

Comment. This case report cites a unique cholecystogastric fistula caused by biliary calculi. The pathologic process of formation of such a fistula has been observed.

Long-standing inflammatory disease of the gallbladder with associated calculi produced surrounding adhesions involving the stomach. Exacerbations of inflammatory reaction occurred, and with obstruction of the cystic duct the stomach wall was eroded. This fistula was incomplete because of an intact gastric mucosa. It should be emphasized that the mucosal ulceration reported by x-ray was not demonstrated in the surgical specimen. This is also evidence that the fistula did not occur primarily as the result of peptic ulceration of the stomach with perforation. The majority of internal biliary fistulas are caused by gallbladder calculi (85 to 90 per cent) whereas only 5 to 6 per cent of these fistulas are the result of peptic ulceration.

This fistula was nearing the stage of completion heralded by the gastric mucosal erosion and hemorrhage. Progression of the process would have released numerous calculi into the stomach which could have been vomited or passed per rectum. Such an event would have facilitated an earlier diagnosis. However, without such obvious factors this patient presented an interesting problem of an incomplete cholecystogastric fistula with intramural gallstones, simulating a gastric neoplasm. (Fig. 1.) This problem has been cited in the literature. Among three other cases reviewed at the University Hospital, one was similar. Operation performed for a gastric neoplasm disclosed a complete cholecystogastric fistula caused by chronic cholecystitis.

SUMMARY

A case of incomplete cholecystogastric fistula has been presented. This case has been shown to be a problem of diagnosis in respect to gastrointestinal hemorrhage and gastric neoplasm.

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Stability Following Hip Resection for Infection

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RESECTION of a hip does not necessarily result in a weak and unstable joint. Two methods of therapy following resection have been suggested, either external support or reconstructive methods to produce stability. Taylor[1] provided a bucket-top caliper and crutches. Sir Robert Jones[2] attached the greater trochanter with its muscles to the remains of the femoral neck after resection of the head. This procedure was later modified by Girdlestone.[3] Milch[4] performed a Schanz osteotomy after excising the femoral head and neck which ensured stability. Another procedure was described by Harmon[5] in which the neck of the femur was reconstructed to articulate with the acetabulum. In accordance with the present trend, a prosthesis might be inserted as a substitute. However, no reconstructive procedures were performed following resection of the hips in the cases presented here because of severe infections of joints. Strong and stable hips developed due to a phenomenon which is described in each case report. These end results were not anticipated, nor were they due to any planned treatment or regimen.

CASE REPORTS

CASE 1. A thirty-three year old white man, a rehabilitation case worker, was admitted on April 18, 1950, as a transfer from another hospital. He had sustained an open, comminuted, trochanteric fracture with an anterior dislocation of the head and neck of the right femur, an open, comminuted fracture of the left tibia and fibula and other fractures following an automobile accident on March 11, 1950. Gangrene of the left lower extremity necessitated an amputation through the middle third of the left femur.

The stump of the left thigh was in good condition. There was a large decubitus ulcer, 8 inches by 6 inches, over the right buttock and sacral area. A sinus tract extended into the right hip joint from which drained seropurulent material. The head of the femur could be palpated indicating a hard mass under the skin. An x-ray taken upon admission (Fig. 1) shows a severely comminuted fracture of the right hip, which was open with anterior dislocation of the proximal fragment.

FIG. 1. Anterior fracture dislocation of the right hip (April, 1950).

Laboratory observations were as follows: white blood count 11,100, hemoglobin 14 gm., sedimentation rate 47, serology negative,

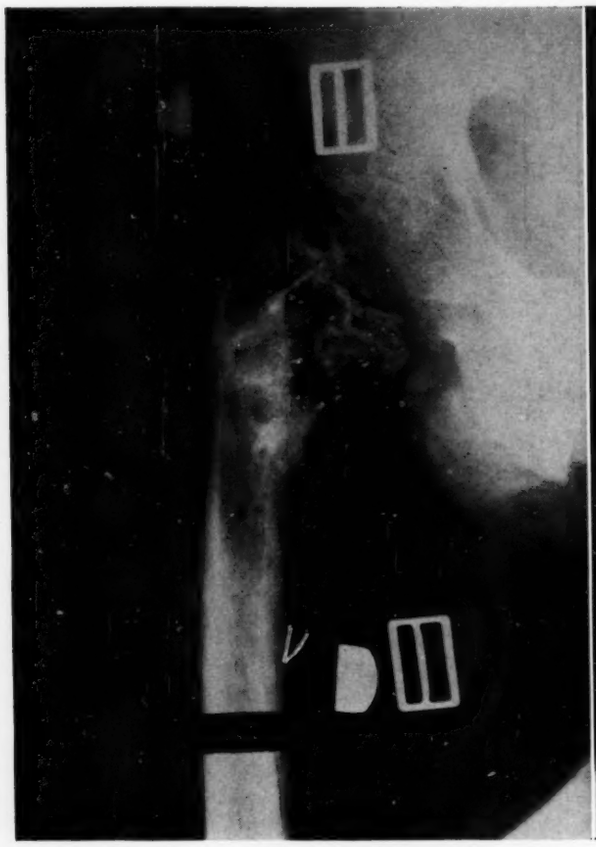

FIG. 2. Illustrates proliferation of dense tissue from proximal end of femur (October, 1950).

FIG. 3. Forty-three months after removal of head and neck of the femur (March, 1954).

protein 5.96 per cent, albumin 3.18 per cent and globulin 2.78 per cent.

The patient was placed on a Stryker frame and skeletal traction was applied to the right lower extremity. Repeat cultures of the sinus tract revealed a mixed infection of Pseudomonas aeruginosa and alpha streptococcus. The decubitus was débrided, a diet high in protein and vitamins was provided and antibiotic treatment in the form of streptomycin 0.5 gm. twice daily and penicillin 150,000 units twice daily was instituted for about eight weeks. Thrombophlebitis of the right saphenous vein which developed on May 2, 1950, responded to anticoagulant therapy.

The sinus tract over the right hip closed by May 15, 1950, and the decubitus ulcer was covered by a sliding pedicle flap of skin on May 17, 1950. An open reduction of the fracture dislocation of the right hip was performed on June 30, 1950. Because of the length of time the dislocation had been present, the hip was reduced with some difficulty and the fracture was secured in position by means of a blade plate. Severe postoperative shock ensued which required intensive supportive therapy. The wound failed to heal and the femoral head, a portion of the acetabulum and the neck of the femur were exposed through a gaping wound from which exuded a profuse purulent drainage. The entire head and neck of the femur and all comminuted pieces of bone, which included fragments of both trochanters, were removed on August 8, 1950, and the wound was packed loosely with vaseline gauze. Four days later the patient was comfortable and up in a wheelchair. The postoperative course was uneventful, and the wound closed spontaneously within ten weeks. It was doubtful that the patient would ever walk with only the support of an artificial limb on the opposite side in view of the large amount of femur which had been removed and the unstable hip which resulted. Insertion of a prosthesis to replace the excised hip or any definitive surgery to produce stability could not be considered then because of the recent infection of that joint. On September 30, 1950, telescoping of the

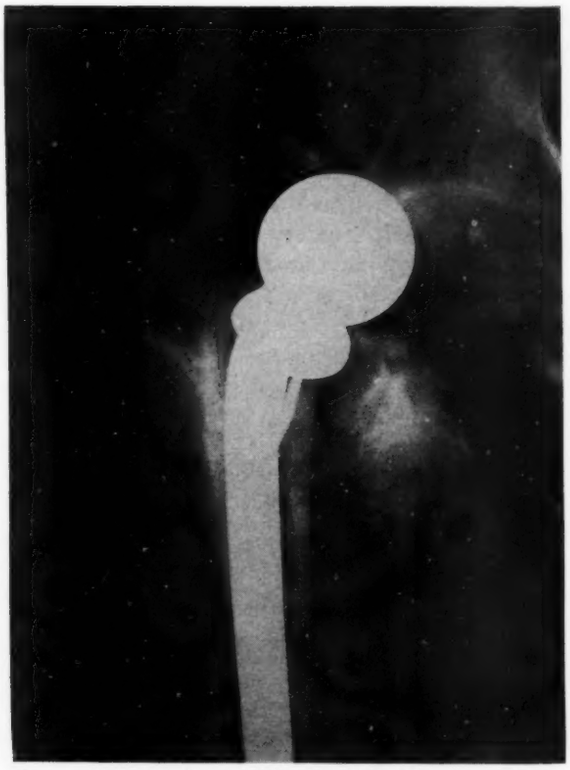

FIG. 4. Prosthesis for the ununited fracture of the neck of the femur after dislocation occurred.

FIG. 5. The proliferation of dense tissue eleven months following removal of the prosthesis (April, 1954).

right hip did not exist and motion did not cause pain. Explanation for this unexpected stability is seen in an x-ray taken then which shows dense tissue maintaining contact between femur and acetabulum. (Fig. 2.) Prognosis for ambulation was changed immediately.

The patient was fitted with an artificial limb for the left lower extremity and taught its use. Soon he also bore complete weight on the right lower extremity—the side of the excised hip. The Trendelenburg test gave negative results. Care given by the Department of Physical Medicine at this time was intensified, and by April 6, 1951, the patient could walk 800 feet and up and down a flight of five steps using Canadian crutches and his artificial limb. A persistent partially stiff right knee and the amputation prevented the patient from progressing more rapidly.

Examination then revealed an adequate left thigh stump with normal hip motion. Passive and active motion of the right hip were identical: Extension 170 degrees, flexion 110 degrees, internal rotation 0 degrees, external rotation plus 20 degrees, abduction plus 20 degrees and adduction plus 20 degrees. The hip was strong and stable. X-rays taken in March, 1954, show the state of the hip as it has been since January, 1952 (Fig. 3). Examination at that time showed motion of the hip to be unchanged and the patient free from pain. He drove his car fitted with hand brakes. He walked with Canadian crutches and often with only a cane. He stated that he was satisfied with the function of the hip, and that if it were not for the amputation he could walk without cane or crutch.

CASE II. A fifty-nine year old white man, known to be a person with tertiary syphilis, was admitted to the hospital on December 10, 1952, because of pain in the right hip. Laboratory observations were within normal limits except for a four-plus Wassermann reaction. An osteotomy had been performed one year prior because of non-union of a femoral neck fracture. A plate and screws, which had been inserted previously for the osteotomy, were removed on January 13, 1953, and an Eicher prosthesis was inserted. (Fig. 4.) The wound failed to heal. A low-grade fever and drainage of a seropurulent material persisted despite antibiotic therapy. Soon dislocation of the

prosthesis developed. Cultures of hemolytic staphylococcus aureus were obtained repeatedly. The prosthesis was removed and a débridement of the hip was performed on May 12, 1953. This wound healed within two months. X-rays taken in August, 1953, show the dense tissue that developed between the proximal end of the femur and the acetabulum. At this time the patient's hip was stable; telescoping was not present. A lift was applied to the patient's shoe and ambulation was thereby encouraged. The Trendelenburg test gave negative results and the patient admitted that pain was negligible. He could walk well with a cane but usually used Canadian crutches. Motion of the hip was as follows: Extension 180 degrees, flexion 130 degrees, rotation 0 degrees, abduction plus 20 degrees and adduction plus 20 degrees. X-rays taken in February, 1954, nine months following removal of the prosthesis, show an increased amount of deposition of bone. (Fig. 5.) Motion and clinical observations, however, were unchanged.

CONCLUSION

Two cases of resection of the hip are described which resulted in strong and stable joints without further surgical intervention. In Case I the resection included most of the trochanters. These cases are not presented to imply that the results were intended and desirable, nor to introduce a new course of therapy for infection of the hip joint; rather, the results represent unusual phenomena that occurred when hip joints were resected following postoperative infection. The proliferation of bone could become extensive enough to produce an ankylosis and represents the same process that often occurs after pyarthrosis of a joint that is not resected. In Case I the proliferation has reached its limit. In Case II further restriction of motion is likely to occur. Postoperative infection is the common factor in both cases. It is therefore concluded to be the direct cause for the bony proliferation and ensuing stability of the hips, although the syphilitic infection in Case II undoubtedly played a large role.

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BOOK REVIEWS

Atlas of Descriptive Human Anatomy. By J. Sobotta, M.D., edited and translated by Eduard Uhlenhuth, M.D. Volume III, fifth English edition translated from the twelfth German edition; volumes I and II, sixth English edition translated from the twelfth German edition. New York, 1954. Hafner Publishing Company, Inc. *Price* $40.00.

The first German edition of this excellent anatomic atlas was published in 1904. The first edition in English was translated and edited by J. Playfair McMurrich, and appeared in 1906 and 1907. During the past fifty years the German version has gone through twelve editions, Dr. Sobotta improving the Atlases up to 1943.

For the past half century Sobotta's Atlas in both the German and English editions has been one of the most popular anatomic atlases in America. Its unavailability during World War II was keenly felt by both medical students and teachers. This new translation is therefore most welcome.

Dr. Uhlenhuth, the present translator and editor, has made no major changes from the last German edition, believing that the real value of a classic may be destroyed by the treatment it receives in the hands of subsequent editors. A work may be so changed in an attempt to modernize it that it would lose the original flavor entirely and no longer deserve to carry the name of the original author.

One important reason for the popularity of the Atlas was Sobotta's original decision to prepare a book in which arteries, veins and nerves of the same layer were illustrated together. Other atlases of the same period illustrated arteries, veins and nerves of the same region in separate plates. Putting arteries, veins and nerves as well as muscles or viscera into one illustration necessitated much more expensive color plates, but these plates have always been the favorite of students of anatomy.

Since the hours devoted to the teaching of gross anatomy have been sharply reduced throughout the United States, and since dissections must be carried out regionally, the student will find Sobotta's Atlas of great help to him inasmuch as the structures of different systems appear in the same illustrations. It is most time-consuming to search for pictures of arteries, veins, nerves and muscles of a given region in different volumes or in different parts of a volume. This Atlas, of course, is still arranged by systems in the text.

Dr. Uhlenhuth has produced an excellent translation of this Atlas. The text is clear, precise and quite readable. For the most part, if a medical student during his course in anatomy reads no more than the text provided with the illustrations in this work, he will have acquired a sufficient knowledge of anatomy to pursue his further medical career.

One feature which some persons may consider a drawback of this Atlas is the fact that all of the terminology is in the original Latin form of the J. N. A. (Jena nomina anatomica). This terminology was adopted by the German Anatomical Society in 1935 at a meeting in Jena, Germany. It was a revision of the B. N. A. (Basel nomina anatomica) adopted in 1895 at Basel, Switzerland, which has been the leading anatomic terminology for the past sixty years. In the United Kingdom and Canada the terminology in use for the past twenty years has been the B. R. (British Revision of the B. N. A.), and in the United States many anatomists have used an Anglicized version of the B. N. A. In this country the J. N. A. has not received the same acceptance as the B. R. and the Anglicized B. N. A.

In order to help the modern medical student who nowadays is not familiar with Latin or Greek, each volume has a chapter at the beginning on the etymology and meaning of anatomic names. These chapters should be most helpful. The most convenient form is to be found in Volume II where all the terms used in this volume are listed alphabetically. In Volumes I and III the terms are arranged by systems. Since the Anglicized version of the B. N. A. in common use in the United States is for the most part merely a transliteration of terms rather than a thorough translation, the student should have no great difficulty in the use of the Atlas if he spends a small amount of time glancing through the chapters on etymology and meaning of terms.

Volume I covers the regions of the body, the skeleton, ligaments, joints and muscles. Since medical students, however, usually study the hard parts separately, the skeleton by itself, and the ligaments and joints after stripping off more superficial structures, Volume I represents an advantage rather than a handicap. Volume II deals with the digestive, respiratory, urogenital and vascular systems, including a number of plates on the heart. Volume III deals with further plates on blood vessels, including the coronary circulation, the nervous system, sense organs, integument and lymphatics.

Volume I contains 180 color and 183 black and white illustrations on full-page plates, and 43 additional partly colored figures in the text. Volume II contains 110 color and 102 black and white illustrations on full-page plates, and 31 additional partly colored figures in the text. Volume III contains 146 color and 142 black and white illustrations on full-page plates, and 67 additional partly colored figures in the text. This makes a total of 1,022 illustrations, of which 454 are in full color and 141 text figures which have one added color. These illustrations provide a full coverage of the essentials of gross anatomy. With the rather complete text provided, a student could get along quite well in his gross anatomy course using only this Atlas, provided that he acquires from other sources some knowledge of anatomic principles.

The value which this Atlas has over the usual textbook is that it never becomes out of date. The value of the illustrations will not diminish and it is one of the few books which the medical student will want to keep, for its usefulness to him in his subsequent career will remain, no matter in what field of medicine he may concentrate his efforts.

NORMAND L. HOERR, M.D.

Babcock's Principles and Practice of Surgery. Edited by Karl C. Jonas, M.D., M.S. (Surg.). Second edition, 1,563 pages, 1,006 illustrations, 10 colored plates. Philadelphia, 1954. Lea & Febiger. *Price* $18.00.

This edition covers the field of surgery in its many aspects. It is a highly authoritative one-volume work. The text has been written by fifty-six active teachers of surgery writing under the editorial guidance of Dr. Jonas, for many years an associate of Dr. Babcock. The sequence of presentation has been changed in this edition; the textmatter has been revised, rewritten and brought up-to-date. The book has been enlarged by more than 200 pages, with eight new chapters and approximately 500 new illustrations. Emphasis is placed on surgical diagnosis and treatment, and all current advances in general surgery and specialties are included.

From every viewpoint this is a much above-the-average work that deserves wide distribution.

Surgery of Repair As Applied to Hand Injuries. By B. K. Rank, M.S. (Melbourne) and A. R. Wakefield, M.S. (Melbourne), with a Foreword by Sir Gordon Gordon-Taylor, K.B.E., C.B., LL.D., SC.D., 256 pages, 184 figures. Edinburgh and London, 1953. E. & S. Livingstone Ltd. (Baltimore, Williams & Wilkins Co.) *Price* $8.00.

This outstanding book is by two distinguished Australian surgeons. Sir Gordon Gordon-Taylor, in the Foreword, informs us that " . . . the authors have derived much of their inspiration and received training from surgeons like Gillies, McIndoe, Kilner and Rainsford Mawlem. It may therefore be reckoned a British Empire work, embodying all that has made British reparative surgery famous throughout the world as well as the special experience which has come the authors' way."

Injuries to the hand constitute a special problem for the majority of general surgeons. Specially trained surgeons in this field are in the minority. The authors have written a book on surgery of hand injuries under present-day conditions. We are informed that "The work is meant primarily for the discriminative interest of those who see and treat hand injuries." The book is based on a wide practical experience covering the past ten years. The authors have had an opportunity to see and study this work in Britain and America. Briefly, the contents covered are: part 1, social significance of hand injuries, surgical anatomy, organization in relation to hand injuries, examination and appraisal of a recently injured hand; part 2, primary treatment; part 3, intermediate treatment; part 4, secondary treatment of hand injuries (general considerations, scar disabilities, secondary repair of deep structures, unsatisfactory amputation stumps and elective re-amputations, reconstructive procedures for mutilating injuries); part 5, special aspects of hand injury.

The illustrations are excellent, some in color. Most scientific writing is written in a dull, colorless style. Now and then one reads a book or an article that has an engaging and flowing

style. The writers of the reviewed book are masters of the English language. This exceptional text insures delighted readers. Our Australian colleagues have offered a solid and exceptionally well done tome.

Experimental Surgery, Including Surgical Physiology. By J. Markowitz, M.B.E., M.B. (Tor.), PH.D., in collaboration with J. Archibald, D.V.M., M.V. SC. Third edition, 851 pages, 554 figures. Baltimore, 1954. Williams & Wilkins Co. *Price* $10.00.

The first edition of this work came out in 1937 and was reprinted in February, 1942. The second edition was published in 1949. There is nothing to be gained in trying to impress the reader who, no doubt, devotes his working hours to experimental surgery. Any book with the background that this has enjoyed over the past seventeen years needs no laudatory review. One does not paint the lily. Suffice it to state that in this edition every effort has been made to keep up to date in this fast growing field.

It is a useful guide to all who do scientific experimental animal surgery and is a fine textbook for students of surgery, both graduate and undergraduate.

To those interested in this subject and to those who devote their full time to experimental surgery, this work will prove a valuable text.

Atlas of Orthopedic Traction Procedures. By Carlo Scuderi, M.D., PH.D. 230 pages, 124 illustrations. St. Louis, 1954. C. V. Mosby Co. *Price* $12.50.

An above-the-average illustrated book written by a recognized authority and designed to " . . . fill a definite gap in orthopedic literature by photographs, line drawings and simple descriptive language."

The book begins with estimated basic requirements for hospital orthopedic traction equipment. It then considers such subjects as care of the skin, care of skeletal traction, care of the patient, hospital bed, hospital mattresses and overhead frames, and goes on to consider the various methods of traction in all forms of orthopedic conditions requiring traction. As noted heretofore, the illustrations are exceptionally good. The accompanying text is to the point and makes clear the purpose of the methods employed.

An excellent text for students, residents in fracture and straight orthopedic services, the nursing profession and physical therapists who work with this type of patient.

Surgical Pathology. By Peter A. Herbut, M.D. Second edition, 893 pages, 528 illustrations. Philadelphia, 1954. Lea & Febiger. *Price* $14.00.

The author fulfills two aims in this work: (1) to consider the subject from a regional viewpoint, (2) to summarize, as far as possible, the newer ideas as reported in the current literature. He has accomplished his purpose. The result is a book that is authoritative, dependable and a ready reference text for those who wish important facts without leafing through a mass of irrelevant detail. Medical students, surgeons and those men who are preparing to take their specialty board examinations will find this volume of inestimable value and assistance.

This second edition has been revised and enlarged by 183 pages. There is a new chapter on the adrenals, and a chapter on the central nervous system by Dr. Bernard J. Alpers. Several subjects have been rewritten, others have been added. The illustrations are well done; 124 new ones have been added and seven others replaced. There is a short consideration of the embryology and histology of each system. At the conclusion of each chapter is a wide and more than ample list of references.

An Atlas of Operations for Trauma. By Otto Russe, M.D. with a Foreword by Lorenz Böhler, M.D. 106 pages, 48 full-page plates. New York, 1955. Intercontinental Book Corp. *Price* $12.50.

The text of this beautifully done atlas is written in German, French and English. The text is on the left hand pages and the illustrations face, as many as ten or twelve to a page. The illustrations are above average, the majority having red lines which make the points clearer. This work depicts the operative methods commonly applied in accident surgery in a series of schematic drawings. In this way one can quickly survey what operations there are, how these are performed and what is required for them. We believe that purchasers of this book will find it very helpful and the money expended well spent.

Ulcerative Colitis and Its Surgical Treatment. By Bryan N. Brooke, M. chir., with a Foreword by F. A. R. Stammers, C.B.E., T.D., B.SC., CH.M. 147 pages, illustrated (some in color). Edinburgh and London, 1954. E. & S. Livingstone Ltd. (The Williams & Wilkins Co., Baltimore, Md.)

We are told in the Foreword that the author of this monograph has gained " . . . what must be one of the largest personal experiences in the country of cases treated by more radical

operation, since, in addition to the 58 patients for whom he has carried out one or more interventions, he has seen many others in whom surgical treatment was considered unnecessary or inadvisable."

The author covers the following subjects: diseases customarily diagnosed as ulcerative colitis, pathologic x-ray and sigmoidoscopic appearances and the nature of ulcerative colitis, complications, a review of surgical procedures and the ileostomy bag, preoperative management and indications for operation, ileostomy, the management of an ileostomy and its complications, removal of the large bowel and complications arising therefrom, results including mortality, rehabilitation, nutrition and pregnancy. This book is well written, with excellent colored illustrations. It is a work of great interest to both physician and surgeon.

Principles of Internal Medicine. Edited by T. R. Harrison, M.D., Raymond D. Adams, M.D., Paul B. Beeson, M.D., William H. Resnik, M.D., George W. Thorn, M.D. and M. M. Wintrobe, M.D. Second edition, 1,703 pages, illustrated. New York, 1954. Blakiston Company, Inc.

The first edition of this large work was published in 1950. Under able editors some eighty-five men of reputation have contributed articles. We read in the preface to the second edition, "The original purpose of this book was to attempt to achieve a balance between art and the science of medicine. The hope of the Editors was to present material which deals with the practical problems of internal medicine today, and to integrate this with those basic principles which will in all probability determine the practice of tomorrow." This blueprint has been molded into an actuality. The contents of the book cover the broad field of internal medicine. Without exception every chapter is very well written.

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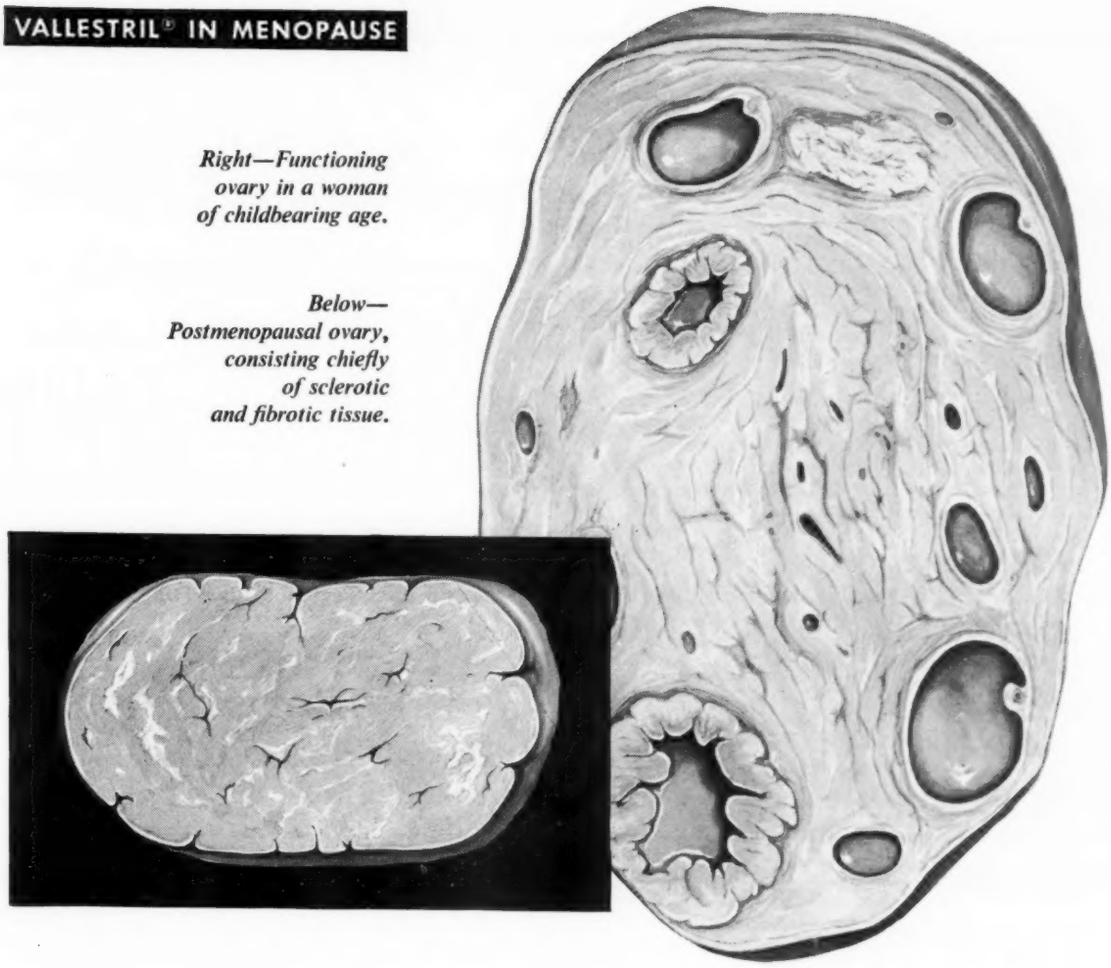

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[1]Sturnick, M. I., and Gargill, S. L.: Clinical Assay of a New Synthetic Estrogen: Vallestril, New England J. Med. *247*:829 (Nov. 27) 1952.

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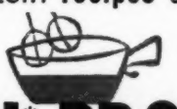

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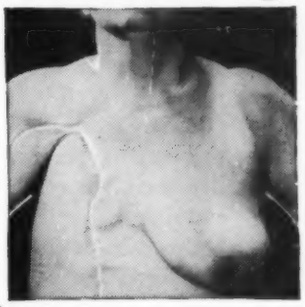

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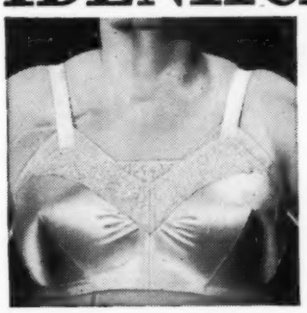

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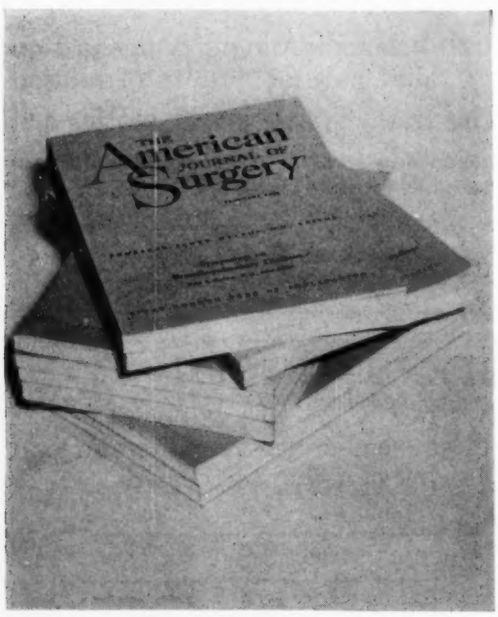

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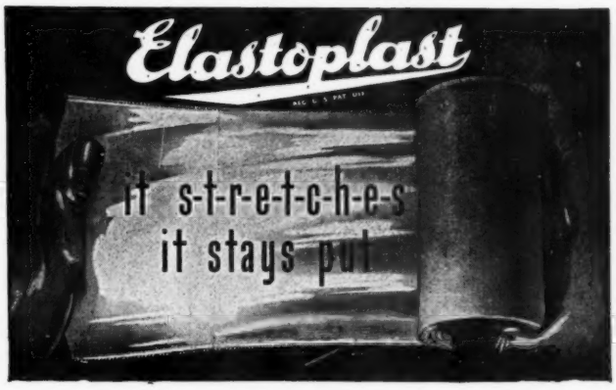

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NOTES AND QUOTES

FUTURE programs calendared by the University of California Extension through its medical extension division in Los Angeles, include a limited 1955 Summer Medical Series. Study topics and meeting dates at the Medical Center on the Los Angeles campus include Surgery of Elbow and Shoulder: July 19, 20; Surgery of Hand: July 21 and 22; Recent Advances in Medicine: July 25 to 29; Basic Technics of Hypnosis: August 8, 9 and 10; Advanced Technics and Application of Hypnosis: August 10, 11 and 12; and Anesthesia: August 29, 30 and 31. Advanced announcement is also made of a fall course in Pediatrics set for October 20 and 21.

Requests for information on these and other courses should be addressed to: Medical Extension, University of California, Los Angeles 24, California.

A unique physical reaction gives a camel more mileage per gallon of water than any other large animal in the world. A camel in the severe heat and the water shortage of the desert can stand to lose an amount of water equal to 30 per cent of its body weight, a Duke University research team told the Federation of American Societies for Experimental Biology.

Other animals die from circulatory failure in hot environments when water loss equals 12 per cent of body weight, Dr. Bodil Schmidt-Nielsen pointed out. The Duke scientist and her husband, Dr. Knut Schmidt-Nielsen, led a year-long expedition into the Sahara Desert during 1953 to 1954 to study the physiology of the camel. Co-authors of the paper and members of the Schmidt-Nielsen expedition include T. Richard Houpt of the University of Pennsylvania, and S. A. Jarnum of the University of Copenhagen, Denmark.

A major reason for the camel's ability to stand such drastic physical change seems to be that water loss has little effect on the volume of plasma in the blood, the scientists said. The camel drinks enough water in ten minutes for complete "refueling," during which there is a marked drop in plasma concentration. Even such a sharp drop produces no ill effects.

THE author of the article, "An Improved Sigmoidoscope for Operative Work," published in the March 1955 issue of the Journal, wishes to acknowledge a reference which was inadvertently omitted: TURELL, R. A sigmoidoscope with proximal and distal illumination. *Surgery*, Vol. 25, No. 4, April 19, 1949.

The Medical Extension Division of University of California Extension in Los Angeles will hold an Anesthesia Seminar this summer on Monday, August 29th, from 9 A.M. to 5 P.M. Dr. John B. Dillon is Chairman of a staff of sixteen.

Topics set for the day include Modern Administration of Ether, Circulation during Anesthesia, and Balanced Anesthesia, with the day's program planned to review and emphasize some of the fundamentals of the physiology and pharmacology involved in clinical anesthesiology.

Information concerning the Seminar, which is limited to 100 students with a fee of $50.00, may be obtained from the offices of Medical Extension, University of California, Los Angeles 24, California.

SURGERY with its classic anatomic forms has perhaps enabled contemporary medical illustrators to "snatch a grace beyond the reach of art."

A handsome portfolio of impressive, colorful new prints illustrating six well known surgical procedures is being offered free to the surgical profession by Ethicon, Inc. Reproduced from original artwork prepared exclusively for Ethicon, this "Portfolio of Surgical Interventions" contains six plates in full color, suitable for framing. Each measures 8½ by 11½ inches, with a 1½ inch border.

The designs illustrate and interpret esthetically the procedure in cholecystectomy; pyeloplasty; gastrojejunostomy; operation for patent ductus arteriosus; colostomy, Mikulicz; and thyroidectomy. The designs are described as a development in the long history of medical art.

"The first records of drawings are those of biological subjects drawn by the cave men of the Paleolithic Period, and medical pictures carved on bone or stone can be seen in our museums today. Greek vase paintings also indicate man's early interest in medical and biological subjects.

CONTINUED ON PAGE 42

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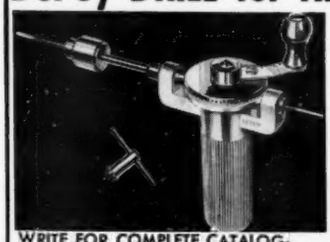

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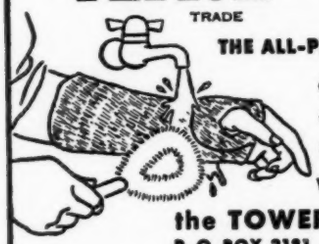

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NOTES AND QUOTES

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Intramedic polyethylene tubing is now being manufactured and distributed by Clay-Adams, Inc. in sterile form. Packaged in tough polyethylene envelopes, the tubing is sold under the Clay-Adams "Intramedic" trade mark and is ready for immediate use as soon as the package is opened. Sterile Intramedic Polyethylene Tubing is sold in the following sizes: PE-50/S36 (36 *inch length*), PE-90/S12 (12 *inch length*), PE-190/S12 *and* PE-200/S12. *Some of the more important uses for these sizes are intravenous therapy, caudal and spinal analgesia, exchange transfusions in the newborn and tube feeding for prematures.*

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PITMAN-MOORE COMPANY has announced a million dollar expansion program at its Indianapolis pharmaceutical plant and on company property near Zionsville, Indiana. Included will be a three-story addition to its Indianapolis plant and a pathology building to be constructed on ground adjacent to the virus research building fifteen miles northwest of Indianapolis. Construction to begin soon at Pitman-Moore's Indianapolis plant will provide added office, production and laboratory space. All mechanical service equipment for the operation of the new facilities will be housed in a penthouse atop the new building.

Plans call for tablets and sterile solutions to be manufactured in the addition. The building will be of special floor and partition construction with air treatment conducive to sterility and dust-free conditions.

The seventh Postgraduate Assembly in Endocrinology and Metabolism sponsored jointly by the Endocrine Society and the Indiana University School of Medicine will be held at Indiana University Medical Center in Indianapolis from September 26th to October 1, 1955. The faculty will consist of twenty-one eminent clinicians and investigators from various parts of the country in the fields of endocrinology and metabolism. The program will cover the various endocrinopathies, with emphasis on the clinical aspects, demonstration of laboratory tests, presentations of cases, and question-and-answer panel discussions. The course is designed to cover the main aspects of diagnosis and therapy in the field of endocrinology and metabolism for the physician in general practice and for those in other specialties who wish to have a general knowledge of this rapidly growing field. A syllabus with brief abstracts of lectures will be available to the registrants at the time of the assembly.

Further information concerning the program can be had by writing: Post Graduate Office, Indiana University Medical Center, 1100 West Michigan Street, Indianapolis 7, Indiana. Registration is limited to 100; tuition fee is $100.00. Arrangements for housing accommodations will be made through the University.

ABOUT three of every five American males who were twenty in 1910—those born in 1890—will still be alive to celebrate their sixty-fifth birthday this year. For women born in the same year the survival record is even more favorable, the comparable proportion being slightly higher than seven of ten.

The foregoing is derived from a recent report by Metropolitan Life Insurance Company statisticians on the increasing chances of survival among Americans which have resulted from the decline in mortality since the turn of the century.

Better chances of survival have come to each successive generation of Americans throughout this period, the report shows, and

CONTINUED ON PAGE 44

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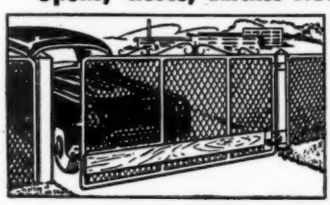

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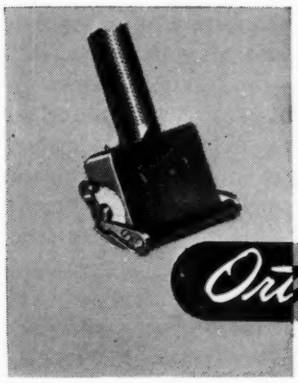

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while the gains have been particularly impressive in early life, substantial progress has also been made at the ages when most men are gainfully employed and when most women bear responsibility for the care of a home and children.

Our younger generations, it is noted, undoubtedly will have an even more favorable record of survival than persons born before the turn of the century, because death rates have been decreasing since 1900 and are likely to decline still further in the future.

Even if current levels of mortality were to remain unchanged, however, better than two of every three men over twenty years of age, and more than four of five women at these ages will survive beyond their sixty-fifth birthday, according to the study. How much more favorable the actual record will turn out to be will depend upon many factors, among them further advances in the medical sciences and how rapidly such advances are extended to all segments of the population.

"These trends in longevity have important social and economic implications for our country," the statisticians comment. "In the years ahead, more and more people will live to the age of retirement and beyond. At the same time an increasing proportion of wives will outlive their husbands."

A three-day International Symposium on Enzymes: Units of Biological Structure and Function, sponsored by the Henry Ford Hospital and The Edsel B. Ford Institute for Medical Research will be held in the auditorium of Henry Ford Hospital, November 1, 2, and 3, 1955.

Interrelationships between enzymology and other fields, notably genetics, physiology, biochemistry and pharmacology, will constitute the general theme of the Symposium. The specific topics for the six sessions will be: Origin of Enzymes, Status of the Gene-Enzyme Relationship, Enzymes and Cell Structure, Enzymatic Basis of Some Physiologic Functions, Cellular Energy Sources, and Regulation of Enzyme Activity. More than thirty internationally known scientists have accepted invitations to participate.

For a copy of the preliminary announcement write to Dr. Clarence E. Rupe, Henry Ford Hospital, Detroit 2, Michigan.

A SEVEN-POINT attack on the problem of rehabilitating and discharging long term patients so they may return more quickly to community life as useful citizens is gaining momentum in Veterans Administration hospitals. The seven programs are outlined in the various medical sections of VA's annual report for 1954, now on sale at the Government Printing Office, Washington, D. C.

The problem arises from the fact that the number of veteran patients with chronic disabilities has been increasing in recent years, resulting in more "frozen" beds for long periods of time. These patients primarily are older World War I veterans.

VA said it is attempting to meet the problem by augmenting medical treatment with the following programs: (1) Medical rehabilitation of the "whole man" so he will be ready, physically and mentally, to leave the hospital. (2) Vocational counseling to determine what job he may fill successfully when finally out of the hospital. (3) Trial visits outside of the hospital to determine whether he is ready again for community life. (4) Foster care in a home other than his own where he can adjust himself to community living as a stepping stone to independence. (5) Work experience in the hospital as part of his medical treatment so he may develop work skills or acquire work experience in preparation for outside employment. (6) Arrangements for home nursing care for the eligible veteran so he may leave the hospital earlier. (7) "Day" or "night" hospital for the patient who still needs hospitalization but who may leave the hospital during the day to look for work or who may leave the hospital at night to stay at home.

The medical rehabilitation program is directed not only to the prescribed treatment of a patient's disability, but also aims to restore him to productive living in the community. By using all components of physical medicine and rehabilitation (physical, occupational, educational corrective, and manual arts therapies), the patient is helped to overcome his disabilities and to make use of his capabilities.

This combined program of medical treatment and rehabilitation has resulted in the discharge of many long term patients whose cases heretofore had been considered hopeless.

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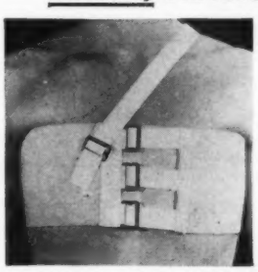

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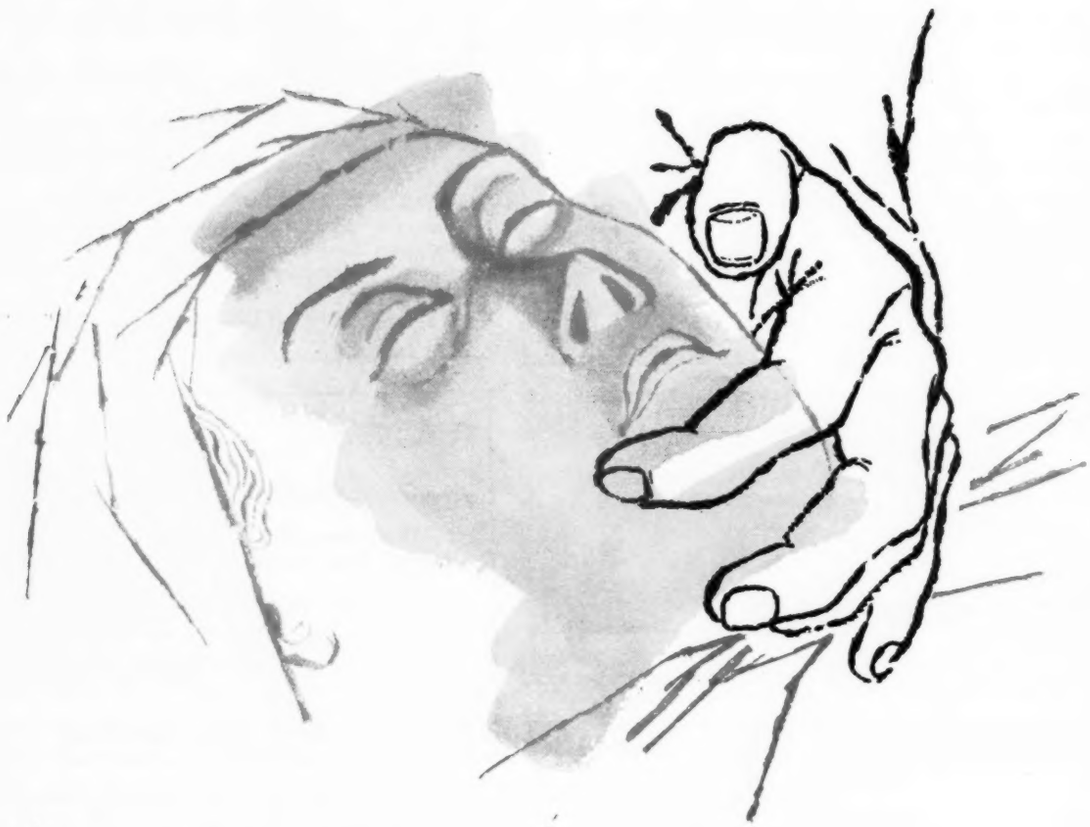

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Auto-Bumper Gate Co.... 43
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Bard-Parker Co., Inc.... 26
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15, 31, 37, *Back Cover*
Cochrane Physicians' Supplies, Inc.... 41
Cook County Grad. School of Medicine 34
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Cutter Laboratories.... 6
DePuy Manufacturing Co.... 41
Dome Chemicals, Inc.... 39
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Insert Facing Page 24
C. B. Fleet Co., Inc.... 14
Freeman Mfg. Co.... 41
Hoffmann-LaRoche, Inc....
Insert Facing Pages 38, 46
Homemakers' Products Corporation.... 27
Identical Form, Inc.... 35
Johnson & Johnson....
Insert Facing Page 16, 17
Kling Photo Corp.... 43
Lederle Laboratories....35, 38
Eli Lilly & Co.... 32
Little Manufacturing Co., Inc.... 45
Medical Aids, Inc.... 43
V. Mueller & Co.... 10
N.Y. Polyclinic Medical School & Hospital.... 34
Notes and Quotes....40, 42, 44
Orthopedic Frame Co.... 43
Parke, Davis & Co.... 21
Murle Perry.... 45
Pfizer Laboratories, Div. of Chas. Pfizer & Co., Inc....12–13
Geo. P. Pilling & Son Co., Inc.... 30
Propper Mfg. Co.... 45
The Radium Emanation Corp....41, 43
Rajowalt Co.... 45
Reed & Carnrick.... 20
Richards Mfg. Co., Inc.... 45
Riker Laboratories, Inc.... 24
H. W. Rutzen & Son.... 41
Seal-Ins Laboratories, Inc.... 41
G. D. Searle & Co.... 33
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The Surgeon's Mart....41, 43, 45
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